

# Effects of Musculoskeletal Dysfunction in Excessive Crying Syndromes of Infancy

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## DECLARATION

I declare that I conducted the work represented in this thesis entitled *Effects of musculoskeletal dysfunction in excessive crying syndromes of infancy* and composed it myself. The work that is presented is, to the best of my knowledge, original except as acknowledged in the script. As a thesis written for PhD by publication, there are contributions made by others as outlined in detail in Chapter 2. This thesis has not been submitted previously, either as a whole or in part, for a degree at this or any other university.



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26 March 2014

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Joyce E Miller

## Abstract

**Background:** Excessive crying (or infant colic) is a common pain syndrome of infancy without any specific known aetiology or effective management and it is costly in both social and economic terms. Many cases result in long-term poor sleep, behavioural problems and parental stress. The biomechanical aspects of this condition lack adequate investigation despite its strong link with assisted and/or difficult births.

**Aims and Objectives:** This research series aimed to (a) investigate the musculoskeletal health of infants with the condition of excessive crying; and (b) determine any relevance of chiropractic manual therapy in its management. Eight studies each with its' own specific objectives investigated relevant research questions which were linked to the overall aims.

**Methods:** The eight separate studies used the following methods: (1) demographic survey of paediatric patients attending a university-affiliated chiropractic clinic; (2) record study to determine the prevalence of side effects or adverse events in the patient group less than three years of age; (3) cohort study to substantiate sub-groups of excessively crying infants; (4) prospective observational study to develop a predictive model using likelihood ratios to forecast the presence of infant colic in a clinical population; (5) validation of a one page instrument to assess clinical outcomes against the gold standard crying diary; (6) randomised comparison trial of two types of chiropractic manual therapy for infant colic; (7) randomised controlled single blind trial to determine efficacy of blinding as well as chiropractic manual therapy in management of infant colic; and (8) case-control study to investigate long-term effects of chiropractic manual therapy into toddlerhood. Each of these studies was novel in the field and the first of its kind.

**Summary of Results:** The studies in this thesis added to the body of knowledge through providing unique evidence for the following: (1) parents are willing to take their child to a chiropractic clinic for treatment and most often do so at the recommendation of a medical professional; (2) chiropractic manual therapy is safe for infants and young children; (3) the existence of distinctive / significantly different subgroups within excessively crying infant syndromes; and (4) chiropractic manual therapy is efficacious in the short-term for these cases as well as having durable utility, tested up to the time of toddlerhood.

**Conclusion:** Chiropractic manual therapy was found to be an appropriate, safe and effective intervention for infant excessive crying. These findings may be clinically useful to provide an option for parents and families of afflicted infants and may lend some guidance to clinicians managing difficult cases. This research provides evidence that sub-grouping excessive crying cases may be important to improve outcomes and this may be helpful to develop inclusion/exclusion criteria in future trials. Further multidisciplinary studies are required to determine whether efficacy can be improved with the addition of cooperative care. Further studies should also focus on musculoskeletal effects of difficult births and the medically unexplained symptoms of crying and associated sleeping problems of infants that cannot be explained by any known injury.

## Contents

List of tables .....	5
List of publications: .....	6
Chapter 1. Introduction/background .....	7
Link between pain and excessive crying .....	10
Proposed aetiologies.....	11
Clinical management.....	13
Mechanism of manual treatment .....	14
What is chiropractic? .....	15
How does chiropractic care fit into the care of infants with incessant crying behaviour? .....	16
Risk implications.....	18
Chapter 2. Aims and objectives .....	21
Cohesion of studies.....	21
Chapter 3. Demographic survey of paediatric patients presenting to a chiropractic teaching clinic .....	26
Context of study.....	26
Chapter 4. Assessing short-term effects of chiropractic manual therapy in treatment of infant colic.....	28
Context of study.....	28
Chapter 5. Safety first .....	30
Context of study.....	30
Chapter 6. Improving our understanding of the excessively crying infant.....	32
Context of study.....	32
Chapter 7. Development and validation of Likert scales to detect change in crying .....	34
Context of study.....	34
Chapter 8. Subgrouping the excessively crying infant .....	36
Context of study.....	36
Chapter 9. Randomised Controlled Trial.....	38
Context of study.....	38
Chapter 10. Long-term effects of chiropractic manual therapy in the treatment of infant colic .....	40
Context of study.....	40
Chapter 11. Summary of Study Findings.....	42
What are the implications of this body of work? .....	45

Toward a more utilitarian name .....	48
Strengths and Limitations .....	50
Personal reflections .....	53
Chapter 12. Proposal for assessment, mechanism and cost-effectiveness of manual therapy for infant crying syndromes .....	56
A. Should infants undergo early musculoskeletal assessment? .....	56
B. Plausibility and mechanism of chiropractic manual treatment for the newborn and infant. ....	59
1. Importance of posture and position in health .....	60
2. Manual treatment to reduce pain .....	61
3. Two proposed mechanisms of manual therapy in infants.....	64
C. What are the costs of chiropractic therapy for the treatment of inconsolable crying? .....	67
Chapter 13. Conclusions .....	73
References: .....	75
Appendix I .....	I
Appendix II .....	II
Appendix III .....	III
Appendix IV .....	IV
Appendix V .....	V
Appendix VI .....	VI
Appendix VII .....	VII
Appendix VIII .....	VIII
Appendix IX .....	IX
Appendix X .....	X
Appendix XI .....	XI
Appendix XII .....	XII

## List of tables

Table 1: Historical Myths of Infant Colic .....	9
Table 2: Musculoskeletal symptoms associated with Excessive Crying Syndromes.....	17
Table 3: Outline of events in a chiropractic office with presentation of infant colic .....	18
Table 4: NICE Guidelines on Colic .....	20
Table 5: Research objectives of each study/publication and contributions of authors .....	24
Table 6: Timing of eight studies investigation chiropractic therapy and infant colic.....	25
Table 7: Findings of publications I-VIII and implication for further study .....	45
Table 8: Additional findings to research questions in studies I-VIII.....	46
Table 9: Defining features of types of excessive infant crying and their names .....	49
Table 10: Similarities in low back pain in adults and excessive crying of infancy.....	51
Table 11 Neonatal birth injuries categorized by severity .....	57
Table 12: Model of mechanism of manual therapy for pain syndromes.....	63
Table 13 Possible reasons for improvement with chiropractic treatment.....	65
Table 14 Costs of routine care for excessively crying infant in the UK per unit (2010 .....	69
Table 15: Costs of specific types of management of infant colic in 2010.....	70
Table 16 Costs of care associated with Miller, Newell and Bolton 2012 RCT for infant colic	71

## List of publications:

**Publication I :** *Demographic survey of pediatric patients presenting to a chiropractic teaching clinic. Chiropractic and Osteopathy 2010; 18:33.*

**Publication II:** *Comparison of short-term effects of chiropractic spinal manipulation and occipito-sacral decompression in the treatment of infant colic: a single-blinded randomised comparison trial. Clinical Chiropractic 2008; 11:4-14.*

**Publication III:** *Adverse effects of spinal manipulative therapy in children younger than 3 years: a retrospective study in a chiropractic teaching clinic. Journal of Manipulative and Physiological Therapeutics 2008;31(6): 419-423.*

**Publication IV:** *Improving our understanding of the irritable infant: an observational study in a chiropractic teaching clinic. Journal Clinical Nursing 2011;21:63-69.*

**Publication V:** *QUIC: Initial validation of an instrument to measure infant crying. Journal Clinical Chiropractic Pediatrics 2011;12(1):843-848.*

**Publication VI:** *Prognostic significance of subgroup classification of infant patients with crying disorders: a prospective cohort study. Journal of Canadian Chiropractic Association 2012; 56(1): 40-48.*

**Publication VII .** *Efficacy of chiropractic manual therapy in infant colic: a pragmatic single-blind, randomised controlled trial. Journal of Manipulative and Physiological Therapeutics 2012; 35(8):600-7.*

**Publication VIII.** *Long-term effects of infant colic: a survey comparison of chiropractic treatments and non-treatment groups. Journal of Manipulative and Physiological Therapeutics 2009; 32(8): 635-638.*

**Permission for use of each article has been requested and received from each journal. The publications are submitted in their original format, as published within the journals. Thus the page numbers of each appendix number (which matches the publication number, e.g., Appendix I heads the first publication, etc.) are as given in the table of contents. However, the page numbers within each appendix are those of the original journal.**

## Chapter 1. Introduction/background

Clinical care in 2013 is steeped in the world of evidence. This thesis provides evidence of new clinical knowledge developed through a substantial body of research which was peer reviewed through the process of publication and supervised by Professor Edwin van Teijlingen. Eight publications which are at the forefront of the discipline of manual therapy use for the excessively crying baby are the basis of this thesis. Copyright permission was requested and received from each journal. This first chapter provides background to the body of work which is systematically described in Chapter 2.

Evidence-based practice (EBP) was initially defined as “the conscientious, explicit and judicious use of current best evidence in order to make decisions about the care of individual patients” (Sackett et al., 1996). EBP recognises that the clinician still must treat patients in the safest and most efficacious way possible even when no gold standard or high level evidence to guide that treatment exists. Practitioners in the field of manual therapy as it applies to paediatric musculoskeletal medicine may be aware that evidence for this type of practice is scarce, poor quality and urgently needed (Gotlib and Rupert, 2008; Gleberzon et al., 2012). This provided the context for the current studies and the research and publications which are found in Appendices I through VIII begin to address many unanswered questions in the arena of musculoskeletal problems of infancy.

Despite musculoskeletal disorders being the leading cause of pain and the second greatest cause of disability around the world today according to the World Health Organization (WHO) (World Health Organization, 2012), the musculoskeletal health of infants has been inadequately studied. Musculoskeletal maladaptation in infants is defined herein as failure of the motor system to respond, or to respond aberrantly to appropriate sensory stimuli due to biomechanical fault (Ferreira and James, 1972; Prechtel et al., 1997; Reher et al., 2008). Normal response patterns are generated when the musculoskeletal system responds appropriately to the central nervous system that mediates sensorimotor integration of the environment and physiological demands. When the musculoskeletal system cannot respond to normal signals due to biomechanical compromise, then the infant’s response to signals may be inappropriate, inefficient, ineffective or aberrant. These responses become characterised as functional problems of infancy and most commonly include excessive crying, inefficient sleep habits and sometimes ineffective feeding (St.

James-Roberts, 2008). Parents usually seek help for these and other problems of infancy. In Europe, 52% of parents seek complementary and alternative medicine (CAM) for their children (Zuzak et al., 2013) and many more seek conventional medical help worldwide (Kemper, Vohra and Walls, 2008). Mothers are the main decision-makers in health care and when taking a child to see a chiropractor (Carlton, Johnson and Cunliffe, 2009).

Little is known about the impact of musculoskeletal dysfunctions in infancy other than they account for a significant use of resources. While half the expenditure on adult health care can be attributed to musculoskeletal disorders (WHO, 2012), the cost in infancy is also high. Morris and co-workers (2001) calculated the cost of infant crying alone as £65 million to the NHS during the first twelve weeks of life, yet with no evidence of benefit to the child. There are many indirect costs among parents and family members as well, including maternal depression, exhaustion, lost time at work and marital disharmony (Bromfield and Holzer, 2008). Many professional resources are procured to help and Appendix IX describes a common plausible (but not prescriptive) flow through health care.

Although the aetiology of crying and sleeping problems of infancy is not known, not least because the infant is not in a position to say, it is reasonable and logical to link these problems to dysfunctional musculoskeletal habitus, by way of opportunities stemming from intra-uterine constraint or a difficult birth which may result in discomfort or pain (Biedermann, 1995; Papousek and von Hofacker, 1998). Although the child's expression is generally interpreted as excessive crying or infant colic, these problems have been termed medically unexplained symptoms (Bakal et. al., 2009) but have both traditionally and more recently been characterised as pain syndromes of infancy (Geertsma and Hyams, 1989; Gudmundsson, 2010; Williams-Frey, 2011; Romanello et al., 2013). Many authors call birth trauma routine and unavoidable but still suggest evaluation immediately after birth to detect problems early to avoid long-term consequences such as chronic pain syndromes (Stellwagen et al., 2008). There is wide agreement that birth is an important time to prevent future disorders for both the child and the mother (Hundley et al., 2012).

Although infant pain is receiving more attention than in the past, it is still an open debate as there is too little research to on the issues of how much pain and what type of pain infants experience. There is a clear gap in the understanding of infant pain. As such, many past understandings about infant pain may actually have been incorrect; those "myths" that are relevant to the current discussion in this thesis are depicted in Table 1.

Babies do not feel pain or are “not in as much pain as they seem to be.”
Infant colic is a syndrome reflecting upset in the digestive system.
Infant colic is a benign syndrome with uneventful recovery by the end of 3 months.
Infant colic is the end-range on a continuum of normal crying.
Infant colic has no long-term effects on the parents or child.
Infant colic is cow’s milk protein intolerance or lactose intolerance.
Infant colic is due to poor parenting.
Infant colic only afflicts the first born and is related to inexperienced parenting.
Boys and girls are afflicted similarly with infant colic and other crying syndromes.
Source: Illingsworth, 1985; Geertsma and Hyams, 1989; Papousek and von Hofacker, 1998; Wolke et al., 2002; Rao, et al., 2004; Miller, 2007; Freedman et al., 2009; Hemmi et al., 2011

**Table 1: Historical Myths of Infant Colic**

More current research into the epidemiology of children’s pain (Johnston and von Baeyer, 2012) recognises that children have pain, a good deal is musculoskeletal in origin, that it causes a burden for both the child and family, that it often becomes persistent and chronic and it is very difficult to measure across age groups and clinical conditions. Musculoskeletal pain is the most common reason for the referral of children to rheumatologists (McGhee et al., 2002) and pain has usually become chronic by the time of referral. Subtle neurophysiological dysfunctions are commonly missed or minimized by clinicians (AAP, 2005).

Some researchers have proposed that spinally mediated reflexes caused by tactile stimulation causing pain sensations are heightened in neonates due to lower thresholds (Fitzgerald and Beggs, 2001). However, the behavioural reaction to pain often used to evaluate the infant’s discomfort cannot be considered accurate primarily because facial reactions develop slowly, advancing over time and age. Therefore, neonate and young infants may demonstrate a diminished physical reaction to pain, despite having an exaggerated physiological response (Fitzgerald and Beggs, 2001). Infant pain is a specialised topic not only because infants are pre-verbal but also because of clinical difficulty in assessing and measuring pain and acknowledging that infants can have pain without apparent or obvious injury (Finley et al., 2005). Even physiological measurements such as heart, respiratory rates and blood pressure may not be useful in this age group,

particularly in persistent pain or discomfort. Observation of infant behaviours of facial expression, cry, body movements, sleep patterns and inconsolability have been found useful but may also be indicative of a stress response and not just pain. Understanding of infant pain is limited in part due to ethical issues which limit invasive investigations in children (Fitzgerald and Walker, 2009), and prohibit study of the above concepts in human infants.

In animal studies, noxious events occurring at the time of pain pathway establishment resulted in structural (musculoskeletal), functional and behavioural alterations (Ren et al., 2004; Walker et al., 2009). The phenomenon of central sensitisation, well known in adults, has also been observed in infancy (Walker et al., 2009). This was demonstrated in long-term changes in response to pain after a difficult Neonatal Intensive Care Unit (NICU) experience (Lidow, 2002). It is not a great leap to propose that neonates who are exposed to multiple stressors including instrumental delivery and invasive procedures during the time that the architecture of pain sensitivity and processing are still “under construction” may develop pain behaviours that persist. This concept is supported by a study (Hermann et al., 2006) that illustrated an increased perceptual sensitisation to pain 9-14 years *after* painful NICU experience in both pre- and full-term infants.

### **Link between pain and excessive crying**

Excessive infant crying has traditionally been termed infant colic. Although the terms have been and continue to be used interchangeably, the term infant colic has been considered inappropriate because it does not describe the aetiology of the crying and it has accrued many monikers including simply cry-babies, excessive crying of infancy, irritable infant syndrome, unexplained infant crying, inconsolable crying of infancy, unsettled infant syndrome or a pain syndrome of infancy. The condition has been studied in the medical literature for at least six decades with the seminal work of Wessel (Wessel et al., 1954) calling it “three months colic” because it was thought to spontaneously remit at 12 weeks of age. That timeline has since been revised upward with remission said to be anticipated at 4, 5 or 6 months of age and other authors stating that it does not remit at all, but behaviour of the infant simply changes as a wider repertoire of responses becomes available as s/he develops (Wolke et al., 2002). These children have been measured and described as continually unsettled at 7- 8 months of age and older (Sanson et al., 1985).

Several research investigations (Wolke et al., 2002; Becker et al., 2004; Rao et al., 2004; Savino et al., 2005; von Kries et al., 2006; Hemmi, 2011) note a long term negative effect of

infant colic from toddlerhood to school age. It has been implicated in maternal depression (Vik et al., 2009), severe stress in the family, difficulties in family communication, general dissatisfaction and sleeping disorders, as well as psychological disorders (Hall et al., 2011). Hence, the excessive persistent crying of infant colic does not appear to be “benign and self-limiting” as some early authors (Wessel et al., 1954) have proposed.

A potential long-term sequelae is not the only reason for concern about the condition. Numerous authors (Carbaugh, 2004; Reijneveld et al., 2004; Crouch, 2008; Minns et al., 2008; Wirtz and Trent, 2008) have found a link between excessive crying and abuse of the infant. Parents simply run out of ways to handle the baby who will not stop crying, no matter how voraciously they soothe. When investigated, parents who abused their child all gave the same reason, inability to stop the crying (Carbaugh, 2004; Reijneveld et al., 2004).

Treatment for inconsolable crying of infant colic requires attention. Despite this being the most common condition presented to clinicians in the first year of an infant’s life, little respite has been afforded these children and their parents. As time has passed, another issue has become apparent. There are fewer extended families surrounding the infant to assist in care and this as well can cause more difficulty to the family than would be the case if grandparents, aunts and uncles were available to help hold and soothe the baby.

Inconsolability of the infant’s cry is the hallmark of this condition and it is often considered that the child is expressing pain or discomfort and has no other way to seek help. Hence, the inconsolable infant is an enigmatic problem with no known cause or cure. The rate of affliction is wide ranging from 20-35% of infants (Hogdall et al., 1991) and this may be attributable in part to difficulty in precisely defining the condition and its aetiology.

### **Proposed aetiologies**

If the aetiology can be established, then an effective treatment may be found. Some authors (Lothe and Lindberg, 1989) have proposed that infant colic can be treated by changes in feeding and that it is caused by cow milk protein intolerance (CMPI). Certainly, there are cases of excessive crying that are indeed caused by an allergy or sensitivity to cow milk. However, if that is the case, the aetiology and treatment are simple and clear; remove the offending substance (from the mother’s diet) or, if formula fed, switch the child to a hydrolysed formula or an amino acid formula so that the offending milk protein cannot cause the irritation. It may be inappropriate to switch to soya protein as one in four children sensitive to milk protein are also sensitive to soya and the potential for hormone ingestion makes it an inappropriate infant food (Businco et al., 1992).

However, if the cause and treatment are simple and clear, then the child's affliction can be easily diagnosed as CMPI and, therefore, is NOT colic or inconsolable crying of infancy (Miller and Weber-Hellstenius, 2013). Further dietary changes, such as increased fibre or lactase, have not been found to be useful (Hall et al., 2011). Although 70% of the adult population has primary lactase deficiency, this generally first occurs at the age of 5-6 years and is extremely unlikely in infancy (Heyman, 2006). Although dietary interventions such as the introduction of lactase continue to be tried, there is little evidence that any formulations have proved any long-term positive effect on the condition (Dupont et al., 2010). Further, it is widely agreed that there is no association between method (breast or bottle) of feeding and infant colic (Evans et al., 1995; Lucassen and St. James-Roberts, 1998).

All children with excessive crying should have a full assessment to be certain there is no disease process causing the problem. However, since research indicates that fewer than 5% have a medical problem that precipitates the crying (Freedman et al., 2009), this creates a confusing picture, screaming baby and fearful parents with no good medical answer in sight.

Although the clinical diagnosis is cloudy, the presenting picture is clear. The excessively crying baby is healthy, thriving and growing. The inconsolable crying starts from 8-14 days of age (Paradise, 1966) and episodes of crying are most common at the end of the day (Lucassen et al., 1998; Soltis, 2004). Excessive crying was originally defined as that which lasted more than three hours a day more than three days per week for more than three weeks (Wessel, 1954). Diagnoses based on time of crying have little utility and more modern definitions accept that parents can report accurately whether or not their child suffers from colic, and this is called the "mother's diagnosis" (Pauli-Pott et al., 2000; Miller et al., 2012). A number of accompanying behaviours have been implicated, for example, passing wind, drawing up of the legs, flailing of the arms and extremities, flushing in the face and general pain behaviours (Illingsworth, 1985) but there is no consistent corroboration of these findings. Research has been unable to establish whether these are actual features of the disorder or of other aetiologies (such as general pain). What is clear is that the actual cause of colic has not been found. Attempts to connect it to the digestive system with a cause of painful abdominal contractions (St. James-Roberts and Hallil, 1991) or gastro-intestinal pathology have been unsuccessful and, if anything, account for only a few cases (Miller and Barr, 1991).

## Clinical management

What does appear to be clear is that this is a behavioural disorder that clearly affects the family as well as the infant. Due to the egregious sequelae and potential for maltreatment of the infant and long-term problems, all types of clinicians feel a need to try to manage the condition (Crouch et al., 2008). Many different types of therapy have been tried to relieve the problem including hospitalisation, pharmacology, behavioural interventions, homeopathy, naturopathic interventions, herbal formulation, dietary interventions and manual medicine. This has resulted in expense but little relief for the families (Morris et al., 2001; Husereau et al., 2003).

Although one out of six children present to the hospital with a severe crying episode (St.James Roberts and Halil, 1991), hospitalisation is not considered appropriate and may even lead to harmful or unnecessary interventions (Savino et al., 2007). Likewise, pharmacological treatments, such as Dicyclomine (an anticholinergic drug) have been found to be harmful (Garrison and Christakis, 2000) with severe adverse effects including respiratory difficulties, seizure and death and this drug has been removed from the repertoire of treatments prior to six months of age. The most common allopathic medication given, Simethicone, has been shown in three double blind studies to have no effect (Garrison and Christakis, 2000). Yet, millions are spent on dispensing it to children each year (Husereau et al., 2003).

Other medications (including Gaviscon, proton-pump inhibitors and acid suppressants) routinely prescribed for gastroesophageal reflux disease (GORD) are commonly given to this age group for excessive crying despite lack of evidence to support their use (Savino and Castagno, 2008). It is important to note that gastroesophageal reflux disease is a completely different diagnosis from infant colic and anti-reflux medications should be preserved specifically for a GORD diagnosis (Hassal, 2012). It has been shown (Sherman et al., 2009) that GORD is a rare pure cause of excessive infant crying and improved differential diagnosis is required. There is emerging evidence that probiotics used to modulate microbiotic intestinal flora in the child may be helpful but more research is necessary to determine its actual efficacy in the pain syndrome of excessive crying (Savino et al., 2010) and for general health.

Other ingested therapeutics such as herbal medicine and homeopathy, botanical supplements and teas have been subjected to few trials and have produced mixed results, raising concerns about adverse effects (Aviner et al., 2010; Thompson et al., 2010). There

are also concerns about their potential to interfere with infant feeding (Capasso et al., 2007; Zhang et al., 2011).

A wide variety of behavioural interventions including car ride simulation, enhanced carrying, routinised uniform daily care and swaddling (Barr et al., 1991; St James-Roberts, 1995; McRury and Zolotor, 2010) have been investigated with insufficient evidence to recommend. Certainly, the myriad of paediatricians, GPs, nurses, midwives, health visitors and others consulted give a good deal of reassurance regarding the disorder's benign nature and helpful tips such as parents getting sufficient rest and respite for themselves and to incorporate family assistance in caring for the child to ease the burden, but without success (Lucassen et al., 1998).

At the same time, chiropractic manual therapy in the treatment of infant colic has shown some promise (Dobson et al., 2012). Moreover, there may be some, if limited, evidence for the use of massage in the first six months (Underdown et al., 2006).

The first time that manual medicine was reported as a treatment for infant colic was by Still in 1910. Since then, parents have sought chiropractic care in increasing numbers (Barnes et al., 2008; Kemper et al., 2008). Good results from manual treatment of infant colic have been reported (Klougart et al., 1989; Biederman, 1995; Mercer and Nook, 1999; Wiberg et al., 1999; Koonin et al., 2002; Karpelowsky, 2004; Hayden and Mullinger, 2006) through the years, but the therapies have not been routinely submitted to randomisation and blinding to decrease bias. Nor have the mechanisms been well explained.

### **Mechanism of manual treatment**

There may be a potential plausible biological mechanism by which chiropractic therapy could work. It is known that pain sensations occur in infants and that the sensory system is intact well before birth and increases in ability to process sensations soon after birth (Buonocore and Bellieni, 2010). Further, pain sensations are most likely amplified in the very young ages and this affects functional movement patterns short-term (Fitzgerald and Beggs, 2001) and long-term (Hermann et al., 2006). If the infant is subject to tense muscles and imbalances in the spine and ligaments, it may be reasonable to postulate that chiropractic manual therapy may alleviate the imbalance, restore normal musculoskeletal function and relieve tension and pain. This is achieved through mild finger pressure to a restrictive barrier. The rationale for this type of care is the theory that well-being is related to connective tissues, including muscles and ligaments and fascia, working smoothly together with the skeletal structure along with the nervous system to integrate and relieve

misalignments and decrease soft-tissue tensions in the body (Nyiendo et al., 1997). This may enhance blood and nerve supply to any areas of dysfunction, thus decreasing sensations of pain. In adults chiropractic care has been shown to reduce pain (Shi et al., 2007).

### **What is chiropractic?**

Chiropractic is manual medicine and is one of the most common types of manual therapies which include osteopathy and physiotherapy among about 40 others (Appendix X) (Owen, 2013). Chiropractors are musculoskeletalists who differ from the other types of manual therapists in that chiropractors are trained as primary contact clinicians and diagnosis along with specific type of manual therapies (WHO, 2005). As such, it is a profession which dedicates itself to the prevention and treatment of musculoskeletal problems of humans of all ages.

The World Health Organisation (2005) defines chiropractic as:

*“A health care profession concerned with the diagnosis, treatment and prevention of disorders of the neuromusculoskeletal system and the effects of these disorders on general health.”*

The chiropractic profession has been in existence for well over 100 years and is the third largest health care profession in the world after general medical practice and dentistry (Mootz et al., 2006). Chiropractors focus upon mechanical stress of the human body and this begins from the time of intra-uterine life and includes passage through the birth canal (Stellwagen et al., 2008) as well as everyday life stresses which can manifest as pain, loss of function and even disability (Nyiendo, et al., 1997).

Chiropractic therapy is demarcated by the use of manual treatment of joints and soft tissues intended to promote the health and well-being of the patient. It may encompass a wide variety of techniques or modalities including chiropractic manual therapy, light touch (hold and release), moderate touch or deeper pressure involving treatment of trigger points, myofascial release, neuromuscular techniques or massage. A list of definitions that describes the various types of therapies, age groups and effects is found in Appendix XI. Touch is the first sense to develop in humans and therapeutic touch therapy has been known and used in health care since the time of Hippocrates or before (c. 460 BC to 370 BC) and continues in use for pain control in modern medicine for even premature neonates (Honda et al., 2013). Significant benefits of chiropractic manual therapy for pain control have been documented in at least one meta-analysis (Moyer et al., 2004). Whether it

functions only in symptom reduction or in global enhancement of over-all health is not known.

### **How does chiropractic care fit into the care of infants with incessant crying behaviour?**

Despite years of investigation, the cause of excessive crying has not yet been found.

Interestingly, the musculoskeletal system has been implicated by specialist neurologists, physiotherapists and orthopaedic surgeons (Papousek and Hofacker, 1998; Biedermann, 2006; Holsti and Grunau, 2007; Gudmundson, 2010) and has resulted in lists of musculoskeletal findings (Table 2) in “colicky” babies and babies in pain and these are remarkably similar to the signs and symptoms that chiropractors have noted in practice over the years (Wiberg and Wiberg, 2010).

Asymmetrical motor function
Asymmetrical occipital flattening
Decreased active cervical range of motion
Fixed supination of upper extremities
Gluteal asymmetry
Hyperextension of cervical spine
Impaired postural control
Increase in cervical tone
Orofacial hypotonia, spitting up/vomiting
Postural asymmetries
Premature verticalisation
Shoulder retraction
Suboptimal quality and character of spontaneous movements
Extended posture
Torticollis
Trunk hypotonia
Unilateral hypertonia of one extremity
Weak cervical flexors
Source: Biedermann, 1995; Papousek and Hofacker, 1998

**Table 2: Musculoskeletal symptoms associated with Excessive Crying Syndromes**

Parents have been making choices that may not yet have reached the threshold of efficacy according to the evidence but may have reached their own threshold to meet a goal to help improve quality of life for the family. As such, the choice of chiropractic care for infant symptoms has been led by parents, in consultation with their GPs (Carlton et al., 2009). From a purely practical point of view, the parent calls upon the clinician to “Do something!” What the chiropractic clinician does is outlined in Table 3.

- The chiropractor takes a complete history including parental concerns, antenatal and birth history, course of growth and development since birth and feeding and elimination history (Hawk et al., 2009).
- The chiropractor observes the gestalt of the infant and family unit and studies posture, habitus, behaviour and seeks a lesion through history and examination.
- A screening for illness is done including heart and respiratory rates, temperature, assessment of growth chart and feeding capabilities, as well as characteristics of temperament.
- The neuro-motor system is screened through reflexes, cranial nerve assessment and movement patterns.
- If musculoskeletal imbalances are found, a treatment plan is formulated based upon treating the most likely cause of the disorder relative to the findings. Without evidence of efficacy, a therapeutic trial is appropriate and 3-5 treatments are recommended as sufficient to determine whether or not this treatment might be helpful to the child's condition (Hawk et al., 2009).
- Symptom response is monitored closely and both the infant's adaptations are assessed and the parental report considered. Very short-term evidence is sought as to whether any change has occurred after the first treatment. If very good effect is reported by the parents after one treatment, this is considered evidence that the therapy may be working (or that it has a powerful placebo effect).
- The treatment plan is then modified to reflect the current state of the infant.
- Treatment continues until parents report total resolution of the condition and the clinician finds no more musculoskeletal maladies to treat (or the child does not improve after a reasonable trial of three treatments).
- Musculoskeletal dysfunctions are reversible at any age but quickly so in the very young population. Parental report has shown (Vallone et al., 2010) that treatment effect, if it transpires, occurs on average after 1.1 treatments and commonly within the first week of care. This will generally be shown in changed signs in the baby's posture and movements and functional patterns (which form the basis of the clinician's findings) as well as behaviours (which are generally the basis of the parental report).
- Infant is released from care, with the occurrence of one of two events:
  - 1) total recovery as determined by the parents and absence of clinical findings after an average of 3-5 treatments, or
  - 2) with only some, little or no benefit from care (Vallone et al., 2010)

**Table 3: Outline of events in a chiropractic office with presentation of infant colic**

### **Risk implications**

Although there is less research than desirable to claim with total confidence that chiropractic therapy for infants is safe, the research to date has shown very few adverse events from care of the paediatric patient, only transient irritability from infant care and one (uncertain) adverse event from colic treatment (Zimmerman et al., 1978; Shafer and

Kaufman, 1992; Pistolese, 1998; Alcantara et al., 2007; Vohra et al., 2007; Humphreys, 2010; Wilson et al., 2012). When put into the context of at least 30 million chiropractic treatments of children annually in the USA alone, adverse events can be considered extremely rare (Lee et al., 2000).

Chiropractors in the United Kingdom and most of the rest of Europe adhere to the Chiropractic Reporting and Learning System (CRLS) of adverse event or near miss reporting and no serious adverse events from infant or child treatment have occurred since its inception in 2006 (Thiel and Bolton, 2006; Wangler et al., 2012). Although some have claimed that adverse effects resulting from chiropractic care of paediatric patients may be under-reported (Vohra et al., 2007), it is unlikely that parents will stand by and watch a child being hurt without a complaint. Any magnitude of problem would certainly be associated with malpractice claims, which are virtually non-existent (Shaw et al., 2010).

There are no guidelines that systematise either the investigation or treatment of pain syndromes of infancy at this time. A medical guideline is a protocol constructed to guide decision making around evidence-based criteria regarding diagnosis, management and treatment in specific areas of health care. These have been used throughout the history of health care but in early times were based on tradition or authority opinion. Now guidelines are evidence-based and an example on colic comes from the UK National Institute for Health and Care Excellence (NICE) (Table 4). In the absence of more specific evidence-based guidelines, it behoves clinicians and researchers to investigate the problem in order to get closer to an answer or produce an answer. Pain syndromes of infancy including the most common problem, excessive crying of infancy provide a window of opportunity into investigation of the musculoskeletal health of infants.

### *Colic*

A baby who is crying excessively and inconsolably, most often during the evening, either drawing its knees up to its abdomen or arching its back, should be assessed for an underlying cause, including infant colic (urgent action).

Assessment of excessive and inconsolable crying should include:

- general health of the baby
- antenatal and perinatal history
- onset and length of crying
- nature of the stools
- feeding assessment
- woman's diet if breastfeeding
- family history of allergy
- parent's response to the baby's crying
- any factors which lessen or worsen the crying.

Healthcare professionals should reassure parents of babies with colic that the baby is not rejecting them and that colic is usually a phase that will pass. Parents should be advised that holding the baby through the crying episode, and accessing peer support may be helpful.

Use of hypoallergenic formula in bottle-fed babies should be considered for treating colic, but only under medical guidance.

Dicycloverine (dicyclomine) should not be used in the treatment of colic due to side effects such as breathing difficulties and coma.

Source: [www.NICE.org.uk/CG37\(2012\)](http://www.NICE.org.uk/CG37(2012))

#### **Table 4: NICE Guidelines on Colic**

This thesis seeks to move the science forward by improving understanding of the defining characteristics and clinical course of the most common condition of infancy, excessive crying, and to investigate through original research, the relevance of chiropractic manual therapy in affecting its clinical course.

Chapter 2 provides aims and objectives of the research and describes the cohesive nature of the research publications included in this thesis. Chapters 3 – 10 contextualise the research studies which are included in Appendices I-VIII. Chapter 11 discusses the research within its context, explores unanswered questions and includes further limitations and reflections. Chapter 12 proposes mechanisms by which the therapy may produce results, recommendations for early musculoskeletal assessments and investigates costs of care. Chapter 13 comprises final thoughts and suggestions for further research.

## Chapter 2. Aims and objectives

Evidence-based practice is the hallmark of all mature health professions and the cornerstone of good clinical practice. The aim of the current series of studies was to first investigate the potential for chiropractic therapy as a provider of care for the excessively crying infant (ECI) and then to systematically provide higher levels of evidence regarding the efficacy of chiropractic treatment for the ECI. The rationale behind the successive investigations was to construct a more rigorous evidence-base for practitioners faced with an excessively crying infant. This plan provides the cohesive basis for these studies; Table 5 outlines the steps, including the objectives of each study.

### Cohesion of studies

This thesis revolves around the clinical presentation and course of the most common condition seen by clinicians in the first year of life, excessive crying. The first study measures the relevant patient numbers entering a university-affiliated chiropractic outpatient teaching clinic. Next, it was necessary to determine whether the available treatment techniques offered any relief for the condition (Study II). Study II showed no adverse events, but a wider investigation into safety of the treatment for very young children was indicated and undertaken in Study III. As there was promise of safety and efficacy in the most general sense, it was appropriate to investigate more deeply the condition and to determine which baseline characteristics best described the excessively crying infant to begin the process of subgrouping in order to improve treatment outcomes (Study IV).

Study V was undertaken to establish the reliability and validity of an instrument developed and used to measure the degree of the problem, as well as any potential improvement and to establish the child's improvement as one of the relevant clinical characteristics. Use of this instrument was invaluable in Study VI which investigated prognostic significance of subgroups of infants according to their clinical characteristics. Study VII provided evidence of efficacy of chiropractic treatment (with parents blinded) for infants suffering from excessive crying. Study VIII provided evidence of long-term change in a group of infants who had been treated with chiropractic manual therapy and showed benefits into toddlerhood. These published studies provide a small but cohesive core to move the evidence base forward in this specific arena.

Objectives	Study/publication	Author contributions
I. To measure the number of relevant cases entering a chiropractic outpatient teaching clinic	I. Demographic survey of paediatric patients presenting to a chiropractic teaching clinic.	J Miller as single author conceived idea and methods, undertook data gathering, data analysis and interpretation and writing for publication.
II. To determine whether chiropractic therapy showed efficacy in the treatment of the excessively crying infant.	II. Comparison of short-term effects of chiropractic spinal manipulation and occipito-sacral decompression in the treatment of infant colic: a single-blinded randomised comparison trial	J Miller conceived the idea, was substantially involved in developing methods, conducted the study in clinic and gave final approval of published version. M Browning was substantially involved in design, analysis and interpretation of data and drafting article.
III. To determine whether chiropractic manual therapy is safe for children less than three years of age	III. Adverse effects of spinal manipulative therapy in children younger than 3 years: a retrospective study in a chiropractic teaching clinic.	J Miller conceived the idea, developed the methodology and wrote the manuscript for publication and guided it through to publication. Kate Benfield assisted with analysis and produced an under-graduate project.
IV. To determine characteristics of the excessively crying infant diagnosed as infant colic	IV. Improving our understanding of the irritable infant: an observational study in a chiropractic teaching clinic	J Miller conceived the idea, developed the instruments and methods and completed the clinical research. B Kvitvaer collated the results and wrote the project and D Newell managed analysis. All contributed to writing of the final manuscript. J Miller completed publication process.
Va. To develop instruments to measure the impacts of clinical problem on both the patient and the parent as	V. QUIC (Questionnaire for unexplained infant crying): Initial validation of an instrument to measure	J Miller conceived the idea, developed the instruments, developed methodology and conducted the study within

<p>well as to measure any change over time.</p> <p>Vb. Validate these instruments.</p>	<p>infant crying</p>	<p>the teaching clinic. A Green assisted in development of methodology in consultation with J Bolton, managed statistical analysis and initial dissertation writing. J Miller wrote the manuscript for publication and completed publication process.</p>
<p>VI. To subgroup excessively crying infants into clinically plausible groups</p>	<p>VI. Prognostic significance of subgroup classification of infant patients with crying disorders: a prospective cohort study</p>	<p>J Miller conceived the idea and methodology, conducted the study in the clinical setting, wrote the manuscript and guided it through publication. D Newell assisted with statistical analysis, interpretation and writing. S Phelps assisted with initial observations, collated data and wrote initial student project</p>
<p>VII. To determine effectiveness of chiropractic manual therapy in the treatment of the excessively crying infant diagnosed with infant colic</p>	<p>VII. Efficacy of chiropractic manual therapy in infant colic: a pragmatic single-blind, randomised controlled trial</p>	<p>J Miller conceived the idea, design and headed the undertaking of the study in the clinical setting, wrote the manuscript and guided it through the publication process. M Browning and N Langlois gave key assistance in the clinical setting. M Torheim Bjelkaroy collated the data and assisted in data processing and did initial project writing. D Newell assisted in statistical analysis and interpretation. J Bolton gave key assistance in study design, analysis and writing.</p>
<p>VIII. To investigate any long-term effects of chiropractic manual therapy in the</p>	<p>VIII. Long term effects of infant colic: a survey comparison of chiropractic</p>	<p>J Miller conceived of the idea, developed the methods, completed the</p>

treatment of infant colic	treatments and non-treatment groups	study in the clinical setting and wrote the manuscript for publication. Lise Haag assisted in data collation and analysis as did Holly Phillips, who analysed control group and wrote under-graduate project report.
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**Table 5: Research objectives of each study/publication and contributions of authors**

This thesis revolves around the clinical course of infant colic in order to improve understanding of its diagnosis, aetiology and management strategies and other concepts and measurements relevant to the condition. This condition is viewed through the scope of the chiropractic profession, but is relevant to any profession that manages the condition. The goal is to contribute significant new insights to the knowledge base to enhance understanding and support appropriate interventions.

An over-arching goal of this research series was to provide tools for clinicians to improve identification and treatment for the excessively crying infant and to provide relief for both the parent and the child whose anxiety and physical tensions, respectively, might be ameliorated. This research may provide background for future researchers to advance the knowledge-base. Certainly, subgroups provide a way forward to understand the individuals afflicted and may assist in improving care for this egregious condition. In consideration of the years of investigation, there is no question that excessive crying syndrome requires further investigation to add understanding to this enigmatic problem with the goal to provide more effective therapies. In all studies, the author of this thesis developed the ideas, initiated the methodologies, wrote for publication and submitted and guided the papers through the publication process, including answering all editorial commentary and managing revisions.

The timing of these studies can be seen in Table 6.

Study	2002	2003	2004	2005	2006	2007	2008	2009	2010
I									
II									
III									
IV									
V									
VI									
VII									
VIII									

**Table 6: Timing of eight studies investigation chiropractic therapy and infant colic**

Study I. Collection of demographic data of paediatric patients attending Anglo-European College of Chiropractic Clinic (AECC) was started in 2002 and continued through 2010. However, the accepted published paper was modified to include data only from 2006 to 2010.

Study II. The randomised comparison trial was developed and carried on in 2003 to 2005.

Study III. The audit to collect side effects or adverse events of paediatric patients under three years of age at AECC collected data from the years 2002 to 2004.

Study IV. The collection of cross-sectional data to discern prognostic characteristics of infant crying took place in the AECC clinic in 2006 to 2007.

Study V. The validation study of a short outcomes instrument against the crying diary took place in April of 2008.

Study VI. The cohort study designed to subgroup crying babies took place from July 2007 through March 2008.

Study VII. The randomised controlled trial of chiropractic manual therapy for the treatment of infant colic took place between October 2007 and November 2009.

Study VIII. The data collection of the case-controlled study of a treatment group and non-treatment group of infant colic took place through the years of 2004 to 2009.

### **Chapter 3. Demographic survey of paediatric patients presenting to a chiropractic teaching clinic**

*Publication I is found in Appendix I: Demographic survey of paediatric patients presenting to a chiropractic teaching clinic. Chiropractic and Osteopathy 2010; 18:33. Introduction and context of study*

#### **Context of study**

Evidence shows that complementary and allied health care usage for children occurs worldwide (South and Lim, 2003; Coulter and Willis, 2004; Nichol et al., 2011; Shmueli et al., 2011; Su and Li, 2011). Often included under the name of CAM (complementary and alternative medicine), the therapeutic category which sees the highest number of children is manual therapy, a generic term which, in this case, includes the two most prominent professions of chiropractic and osteopathy (Barnes et al., 2008).

A working definition of CAM is offered by the USA National Institute of Health (South and Lim, 2003):

*“CAM is a broad domain of healing resources that encompasses all health systems, modalities and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society.”*

Profiles of children who present to CAM are commonly investigated (Su and Li, 2011). A study of the demographic profile of the paediatric patients who presented specifically to a chiropractic clinic was thought to be useful as previously, most surveys were national in nature. Other authors (Pohlman et al., 2010) have suggested that chiropractors who have a special interest in paediatric patients commonly see a greater number and younger paediatric patients. Hence, it was considered appropriate to investigate the ages, conditions and reasons for presentation to a university affiliated chiropractic teaching clinic on the south coast of England and this resulted in a survey which constitutes Study I. A very young population (less than 16 weeks of age) most commonly recommended by a health care professional, was presented most frequently for the condition of excessive crying and musculoskeletal disorders.

Although this study goes some way toward defining the population presenting to a chiropractic teaching clinic, there are still unanswered questions, such as:

What is the socio-economic profile of those patients presented for care? Is there any difference in the socio-economic profile of the infant patients from the adult patients?

Is there anything unique about the parents, in education, age, profession or previous usage of CAM therapies?

Was there dissatisfaction with previous treatment?

What was the child's perceived health status (excellent, good or poor)?

What was the birth history of the child?

What modalities were used to treat the child?

What was the outcome of the care?

Were the families satisfied with treatment?

Had the child visited other CAM therapists prior to this clinic?

Were other CAM therapies used at the same time as attendance at the clinic?

Is there a difference between chiropractic users and non-chiropractic users?

How many treatments were given?

Were there other factors associated with CAM usage?

Does the child's primary practitioner have awareness that the child was presented to the chiropractic clinic?

Since this was a teaching clinic, was the population presented here unique compared to another private chiropractic clinic?

Certainly, the preponderance of unanswered questions limits the use of this data, along with the inherent bias of this data coming only from one clinic and being dependent upon the recall of parents. Despite bias inherent in this type of data collection, 10% of the data were checked for accuracy during the collation process, providing some additional assurance of accuracy. Also, these data were collected for ten years, but only the data for the final five years were utilised in the published journal article. However, the long-term collection did allow corroboration and checking of data points throughout the study.

What this study did do was provide an answer to the question, 'are there sufficient infant patients in this clinic to undergo further, more detailed investigation into the problem of the excessively crying infant?' The answer was yes, thus providing a population base for other studies.

## Chapter 4. Assessing short-term effects of chiropractic manual therapy in treatment of infant colic

**Publication II is found in Appendix II:** *Comparison of short-term effects of chiropractic spinal manipulation and occipito-sacral decompression in the treatment of infant colic: a single-blinded randomised comparison trial. Clinical Chiropractic 2008; 11:4-14.*

### Context of study

This study was undertaken to investigate (while avoiding an ethical dilemma of a non-treatment group) whether there was any basis for the efficacy of chiropractic treatment for children as declared in previous trials (Klougart et al., 1989; Mercer and Nook, 1999; Wiberg et al., 1999). It was unusual in that it tested two manual interventions. The decision to perform within-group as well as between-group analysis was made in order that the trial would have less difficulty with recruitment of subjects and would avoid complex ethics regarding the deprivation of care to infants with a condition with known short and long-term negative sequelae (Rao et al., 2004; Reijneveld et al., 2004; Wolke et al., 2002). However, this resulted in a major impediment. Without an untreated control group, it is impossible to determine whether the significant improvement found secondary to treatment may have occurred with time alone. That said, the time period of the trial was considerably shorter than the natural history of the disorder, considered to be four to six months (Papousek and von Hofacker, 1998; Clifford et al., 2002). This trial has rightly received much criticism for the lack of a non-treatment arm or pure control group (Ernst, 2009). However, this study design was part of a process to build an evidence base one piece at a time, avoiding any harm to children. It was premediated to avoid putting children and families into placebo groups which would markedly delay treatment and might put them at risk (Carbaugh, 2004).

The analysis of testing two different types of chiropractic manual therapies was beneficial as the traditional and classic press-and-hold low force manipulation technique seemed to perform better than the non-traditional more subtle distraction technique, providing a sound rationale for choosing the former technique for further efficacy trials. Although both groups slept better at the end of the 14-day trial, those receiving classic chiropractic treatment improved in sleep almost twice as much and were 20% more likely to recover than the other group and improved more quickly with fewer hours and episodes of crying than the group receiving the non-traditional method. Although these differences might be considered small, they may not be subtle to the family where speed of recovery and shorter crying episodes and longer sleeping episodes are desirable. Nevertheless, there are

significant limitations in such a trial including strict inclusion criteria, inexperienced clinicians (which could also be a strength of the technique used) and the possibility of short-term fluctuations in crying, all of which are included in the discussion of the paper. A strength of this study was randomisation of the subjects. However, usage of opaque envelopes opened at the start of treatment is no longer considered sufficient separation of the treating clinician from the randomisation procedure. A limitation was that the randomisation did not take place in blocks which would have allowed random stratification and prevented any prediction of group by the treating clinician. This limitation was corrected in the second randomised trial.

## Chapter 5. Safety first

**Publication III is found in Appendix III:** *Adverse effects of spinal manipulative therapy in children younger than 3 years: a retrospective study in a chiropractic teaching clinic. Journal of Manipulative and Physiological Therapeutics 2008;31(6): 419-423.*

### Context of study

Paediatric manual therapy (PMT) has become an increasingly popular form of treatment for infants and young children; this type of treatment has the highest utilisation of all CAM therapies for children (Barnes et al., 2008). The specific brand of PMT in this study is chiropractic treatment.

It has been recognised that chiropractic care can have side effects in the adult population, although most are mild, benign and short term, requiring no additional medical care (Senstad et al., 1997; Haas et al., 2004; Haynes et al., 2012). Further research is indicated for assessment of risks of chiropractic treatment in the total population and the chiropractic reporting and learning (CPRLS) system is in force throughout Europe to collect such data (Thiel and Bolton, 2006). Children are included in this population and there have been no reports to date of significant adverse events (Wangler et al., 2012). A study by Humphreys documents a low rate of adverse events in the paediatric population being treated by chiropractors (Humphreys, 2010).

However, vigilance is required to assure safety for all types of treatments for children, particularly in the case of infants treated for excessive crying, simply due to the common presentation. The field of medicine is particularly good at collecting information on side effects and publishing this information to maintain safe practice. For example, there is evidence of serious extrapyramidal dysfunction after the usage of domperidone and seizures and death after the use of dicyclomine, two medications prescribed to treat infant colic (Klassen et al., 2008; Garrison and Christakis, 2000) and hence, less usage of these medications for infants under 6 months of age is recommended. This is a classic example of good practice in patient safety.

It is known to be difficult to “prove” safety of any particular therapy. What is likely is that any therapy with the power to heal has the power to hurt as well. There are risks to all therapeutic procedures and products and the safest treatment may be no treatment at all, at least in a self-resolving condition. However, parents come to a chiropractic clinic for more than reassurance and evidence supports that they have received reassurance from

other clinicians without direct benefit on the condition (Morris et al., 2001; Husereau et al., 2003). It was decided that an audit of the paediatric records under 3 years of age in the chiropractic teaching clinic to determine side effect rate would be a useful endeavour. This was based upon a premise that it is unlikely that any parent will see their child hurt and not register concern. Further, interns, in their educational years are known to be good historians and documentarians (Rosen et al., 2004) and it was expected that the records would be complete and accurate. Despite the expectation of accuracy, data checks were carried out as this is good practice in research design. Data entry rules for missing, illegible or ambiguous data were set in advance and double data entry was done prior to analysis to ensure accuracy as this could be checked in an automated fashion. This is considered appropriate for any data that is anticipated to be used for publication and, as such, this was an additional strength of this study.

There are many limitations in such a study such the reliability of parental report, loss to follow-up and reliability of records and these are included in the discussion of the study.

There are other ways to document adverse effects of treatment and it has been recommended that side effects of care be particularly noted in clinical studies of children, especially randomised trials (Ioannidis and Lau, 2001). This procedure was carried out in the two randomised trials that were conducted in this clinical setting (Browning and Miller, 2008; Miller et al., 2012), which likewise demonstrated a good safety record with no negative effects of treatment. Health care is not known for completeness of safety reporting in randomised trials (Ioannidis and Lau, 2001) and work was done to overcome these deficits in the current studies (Browning and Miller, 2008; Miller et al., 2012). In fact, side effects were documented in all studies where it was possible in this study series. This is considered good practice.

## Chapter 6. Improving our understanding of the excessively crying infant

**Publication IV is found in Appendix IV.** *Improving our understanding of the irritable infant: an observational study in a chiropractic teaching clinic. Journal Clinical Nursing 2011;21:63-69.*

### Context of study

Diagnosing the crying baby has presented clinicians with a conundrum for decades (Douglas and Hill, 2011). Although it is clear that very few excessively crying infants have a life-threatening illness (Freedman et al., 2009), further clarity as to aetiology of the crying is notably lacking. Defining characteristics, if not exact aetiology, would be a first step toward subgrouping infants afflicted with the condition. Therefore, the rationale for this study was to determine which characteristics could reliably be associated with infant colic.

This was a novel study which used all characteristics which had previously been associated in the research literature with infant colic and surveyed over one thousand parents who presented with infant crying and asked them to tick which characteristics were representative of their child. By applying logistic regression, the risks for the condition could be suggested. A nomogram (a predictive tool often used in health care (Gorlia et al., 2008) was used to demonstrate the association between the clusters of features elicited. This was the first time that an attempt was made, using a large sample, to sequester the specific features that most correlate with the affliction. An important feature of this work is that it moved the clinical science beyond a diagnosis based on time of crying, three hours a day, which is much less specific and thus less utilitarian.

Other researchers (Douglas et al., 2011) have suggested a new way of understanding this condition using complexity theory in an attempt to make sense out of relationships of the multiple features of the infant's behaviour. These authors suggest that parents complain of lack of accessibility to any type of helpful health care, along with inconsistency of advice when they do access clinical help and this is because clinicians do not understand the parameters of the condition. They point out that help should be sought early before the behaviour problems become entrenched in the child and stress builds within the family unit. It stands to reason that the earlier the problem is identified, the sooner it can be dealt with appropriately.

It was the aim of this research to demonstrate specific features of the excessively crying baby that could be recognised early. Another main objective was to facilitate further sub-

grouping of excessively crying babies. Sub-grouping would facilitate a direct focus on the specific condition, rather than the amorphous group defined by crying time that constitutes the most commonly used diagnostic feature today.

Despite the weaknesses inherent in such a study, including the specific type of population which presents to this atypical clinic, the maternal preconceptions of the condition and the relatively small number of infants who presented without the condition (all of which are detailed within the study itself), these findings can be used in a preliminary way to begin the important process of subgrouping the excessively crying infant. The strengths of this study were (a) population of more than a thousand subjects; (b) routine clinical practice; (c) broad range and large number (n=52) of potential variables; and (d) which were statistically honed to a relevant few risk factors (n=7) for further study. This investigation provided a new way to identify and define excessive crying syndromes of infancy which moved beyond the single parameter of crying time which could be considered too close to the norm to be clinically useful.

## Chapter 7. Development and validation of Likert scales to detect change in crying

**Publication V is found in Appendix V.** *QUIC: Initial validation of an instrument to measure infant crying. Journal Clinical Chiropractic Pediatrics 2011;12(1):843-848.*

### Context of study

Outcome measures that help guide clinical practice are important to determine patient benefits. There is always a need to assess the extent of a clinical problem and degree of change over time (Stucki et al., 1996; Hurst and Bolton, 2004). Excessive infant crying is a complex clinical problem and involves both the child and the parents. Therefore, it is appropriate to develop scales to assess any clinically meaningful change that occurs over time within both. Since excessive crying is neither life-threatening nor expected to completely resolve within a short space of time, a scale that is sensitive to measure small but significant changes is important. It must be sufficiently responsive to capture change that occurs before the natural history of the condition moves toward resolution. The scale must be also be practical and easy to use by busy families.

Validity is key to reliable usage, so a gold standard (something established as a measure to which other similar things should conform [Dorland's Medical Dictionary, 1991] was needed against which the scales could be measured. The crying diary meets these criteria. Multiple dimensions including crying, sleeping and associations with parental distress were compared over time. The completion of the crying diary was contemporaneous and completed on an hourly and daily basis and the Likert scales were completed during a clinical visit, when a copy of the crying diary was also made. A Likert scale is a psychometric scale commonly used in questionnaires, and is the most widely used scale in survey research. These two instruments were then statistically tested by Pearson's correlation coefficient and associations were found between the report on the crying diary and the Likert scale for the amount and distress of crying.

Considering the fact that change scores are often difficult to interpret (Stucki et al., 1996) the decision to compare the Likert scale to the crying diary, which is very straight forward to interpret, was helpful in making this a clinically useful study. Also, it should be noted that the crying diary has been validated for accuracy in parental report and is considered the gold standard for comparison (Barr et al., 1988).

However, there are also weaknesses in comparing two different outcome measures. For example, the parent's response may be biased on a scale completed on a subsequent day compared to a diary which is contemporaneous. Limitations are discussed within the published paper, as well.

It must be noted that an outdated instrument was published in the report. The correct instrument can be viewed in Appendix V (QUIC II). However, all of the data values presented are correct and that error did not affect the content of the published work. It is the illustration only that was incorrect. One particular strength of this study was that validation of the instrument took place in two separate populations, a private clinic as well as a university-affiliated clinic.

Defining whether change is meaningful and clinically significant or not has been debated for some time (Jacobson and Truax, 1991) but it is suggested that a responsive, quick and easy-to-use change scale may be helpful in making a clinical judgement as to the usefulness of treatment. Providing a clinically useful instrument to accurately measure change in parental stress and the infant's condition was the aim of Study V.

## Chapter 8. Subgrouping the excessively crying infant

**Publication VI is found in Appendix VI.** *Prognostic significance of subgroup classification of infant patients with crying disorders: a prospective cohort study. Journal of Canadian Chiropractic Association 2012; 56(1): 40-48.*

### Context of study

In order to further investigate the excessively crying infant, it now seemed that the only way forward in alleviating suffering in this large and amorphous group was to identify specific characteristics which have the potential to separate them into more cohesive and identifiable sub-groups that might facilitate quicker identification and more effective treatment. Subgroups are used to divide patients by demographic profile or other characteristics into subsets in order to determine whether there are groups where treatment is either more beneficial, more effective, or even harmful (Scott and Campbell, 1998). In this context, beneficial indicates any perceived help to the patient while effectiveness is indicative of an improved clinical course that is significantly better in one group more than another. After conducting Study IV which identified specific features of infant colic, further investigation was necessary to identify whether there were any sub-groups where chiropractic treatment might be helpful and not harmful or vice versa.

There are two ways to determine subgroups. The first is to identify the group with baseline characteristics, prior to the start of a study. The second is to isolate the subgroups based upon unique or differing reactions to the treatment. The first might be considered less biased and hence, *a priori* subgrouping was used in this study. In addition, post-analysis subgrouping was used to inform unique aspects of each cluster. However, the post-analysis was not unplanned (which, according to Scott and Campbell in 1998 has more likelihood of resulting in selection bias). Instead, the statistical analysis was pre-planned, based on biological plausibility and no overall statements of treatment effect were made. Efforts were made to include expert opinion relative to sub-grouping. This included contacting authorities in the field (St.James-Roberts, Wiberg and Wiberg, Williams-Frey) as well as consultations during conferences with other authors, researchers and clinicians. It was thought that the wider the viewpoint, the more likely to establish plausible *a priori* subgroups.

Treatment efficacy could not be ascertained from this type of study because of lack of randomisation. Moreover, the aim of the study was to provide evidence for sub-grouping,

rather than prove therapeutic effectiveness, although it might give guidance in that direction.

Despite *a priori* decisions, it should be noted that it is also possible to uncover a subgroup effect not recognised prior to the start of the study. Certainly, in this study, it was not anticipated that there might be a subgroup with a better response to chiropractic therapy than infant colic, since past research has indicated some effectiveness of manual therapy for that condition. The sub-group irritable infants of musculoskeletal origin (IISMO) showed some indications that manual treatment had better effect than with infant colic. This is merely a trend; it has never been shown in other trials. The effect was found in post-analysis and contributed to the discussion of the mechanism of action or biological plausibility in that some conditions are so clearly musculoskeletal in origin it cannot be denied, whereas the link of infant colic to biomechanical fault is a more current and questionable concept (Wiberg and Wiberg, 2010). This discovery raises the possibility that clinical trials of infant colic may have included infants with other diagnoses, who should have been excluded. This study should be helpful to other studies in determining their inclusion and exclusion criteria.

Another aspect of this study was the attempt to capture the parent's stress level as a parameter of distress within the mother/infant dyad and as a clinical outcome measure. The patient's viewpoint and self-report (Fischer et al., 1999) have been found to be useful for some time in medical care and retrospective reports more sensitive to change than serial reports. It was retrospective (end of treatment) change which was assessed in our subgrouping trial. Hirji and Fagerland in 2009 outlined the importance of outcome based sub-group analysis, which has been used in our trial. A strength of this trial was block randomisation which is a conservative method to assure that the treating clinicians cannot guess the group to which any particular patients can be allocated.

Despite these strengths, there were significant weaknesses in this trial, including sampling bias, maternal reporting bias and the confounding effect of natural history, which are discussed within the publication.

## Chapter 9. Randomised Controlled Trial

**Publication VII is found in Appendix VII.** *Efficacy of chiropractic manual therapy in infant colic: a pragmatic single-blind, randomised controlled trial. Journal of Manipulative and Physiological Therapeutics 2012; 35(8):600-7.*

### Context of study

The highest quality evidence in making treatment decisions comes from systematic reviews of randomised controlled trials (RCTs) (Sackett et al., 2000). RCTs are considered the gold standard of efficacy research and the power of the RCT comes from the randomisation as it is pure chance as to which patient goes into which arm of the trial. This procedure overcomes selection bias which would occur in studies where patients volunteer to participate in a study with a specific type of treatment. Although all types of research are needed, including the lowly case study (Cabán-Martinez, 2012), it is the RCT which actually provides proof that a therapy does what it purports to do. Very few RCTs have been conducted by chiropractors in the paediatric population (Gleberzon et al., 2012).

That said, RCTs are considered more reliable if the patients are blinded, otherwise the mere promise of a new drug or treatment might have such a strong placebo effect that the patient will get better due to hope or some unrecognised process, rather than the treatment. Ideally the clinician is blinded as well, as doctors can be biased, too. However, it is well known that some therapies are difficult to blind, such as surgery, acupuncture and manipulation.

The difficulty in blinding with manual therapy has been a problem for a long time and this is the primary reason why most RCTs of infant colic have not been blinded. It is impossible to blind the therapist as they will know whether or not they gave treatment. However, it is possible to blind the patient, or in this case the parent. It is considered that all infants are blinded as to whether or not they had treatment as they do not possess the cognition to make considerations about treatment or non-treatment (Haugen et al., 2011). It is at least theoretically possible that they might pick up the “vibes” from the parent, however, if they know whether or not treatment was given. Therefore, the parent is the one who is blinded in these studies, although it is difficult because of a governing body mandatory requirement preventing separation of child and guardian (General Chiropractic Council, 2010).

Six earlier studies (Mercer and Nook, 1999; Wiberg et al., 1999; Karpelowsky, 2004; Koonin, 2005; Hayden and Mullinger, 2006; Browning and Miller, 2008) testing manual treatment

for infant colic have shown a positive result. One did not (Olafsdottir et al., 2001). Olafsdottir's study is the one trial that attempted parental blinding and whether true or not, this has been considered to be the reason for the difference in results. Therefore, it was necessary to do another blinded trial in order to continue to test the power of blinding in this type of care.

Hence, the 7<sup>th</sup> study in this series was conceived with the goal of overcoming weaknesses from the other trials. It was not possible to overcome some specific weaknesses of the Olafsdottir trial because this trial did not divulge sufficient detail to understand the actual procedures of the study. Lack of transparency in scientific trials creates problems for others who wish to overcome specific sources of bias; however, bias is, perhaps, inevitable, no matter how well designed the study. The aim of this study was to reduce as much bias as possible in assessing therapeutic benefit of chiropractic treatment for the infant patient suffering from excessive crying.

Although blinding is a key and important aspect of any scientific trial, it has been previously thought that all parents of new-borns are essentially "blind" to whatever type of treatment is afforded because of lack of sleep, the new and unfamiliar context in which they find themselves and their lack of understanding of the treatments. Their only benchmark is whether or not the child gets better. As they often come to manual therapy late in the context of the condition (Appendix IX), after consulting several clinicians and being disappointed by multiple treatments, parental hopes may be lower for chiropractic treatment than for any other therapy they may have tried.

A strength of this trial was block randomisation which is a conservative method to assure that the treating clinicians cannot guess the group to which any particular patients can be allocated. A further strength of this study was parent blinding. No difference was found in effects from treatment whether the parents were blinded or not. It can be argued that there is added strength to the result when the method changes (blinding versus non-blinding) and the results are the same. Thus, it may be appropriate that other trials which were not blinded be re-interpreted in light of new information from this trial.

Although every effort was made to eliminate bias, this was not possible. This trial, like all RCTS suffers from external validity and in the peculiar case of this trial, its pragmatic approach in a routine clinical setting. These are discussed in detail within the published paper.

## Chapter 10. Long-term effects of chiropractic manual therapy in the treatment of infant colic

**Publication VIII is found in Appendix VIII.** *Long-term effects of infant colic: a survey comparison of chiropractic treatments and non-treatment groups. Journal of Manipulative and Physiological Therapeutics 2009; 32(8): 635-638.*

### Context of study

Several studies demonstrate a negative long-term sequelae in older children who suffered from infant colic as a baby (Rautava, 1995; Papousek and von Hofacker, 1998; Wolke et al., 2002; Becker et al., 2004; Rao et al., 2004; von Kries et al., 2006; Hemmi, 2011). These risks start almost immediately in the early weeks of life when not only are infants with colic at increased risk of being taken off breast feeding in the hopes that formula feeding will stop the crying, but they are often put on solids very early, without benefit and with potential harm (Howard et al., 2006)

It is no longer accepted that infant colic is transient and harmless. Rather, it increases the risk of behavioural problems in childhood (Hemmi et al., 2011). Children who had suffered from colic appear to have decreased capacity for self-regulatory behaviour for months and even years after the colicky episode. For example, Rautava et al., in 1995 found significant differences in family functioning in post-colic toddlers versus children who did not have colic as infants.

Although there are multiple studies showing long-term behavioural problems in children who suffered from colic in infancy, what has not been investigated is whether successful treatment has any effect on the long-term ramifications.

Within a student project, questionnaires were sent to 129 families three years after their infant had been treated for colic in a chiropractic teaching clinic. Results indicated that those who had been treated successfully (by parent report) had significantly fewer temper tantrums and sleep disturbances compared to findings reported in the research literature (Hagh, 2005). The study was not submitted for publication because it did not include a control group for comparison of children who had had no treatment and it was felt that the bias may, therefore, be too great.

This gave rise to Study VIII, a comparative study. Approximately 200 children, all between 2 and 3 years of age, were surveyed with half having had successful chiropractic treatment for excessive crying and half having had no treatment. The results showed that children

treated (in the experimental group) displayed significantly less disruptive behaviour than the control group at 2-3 years of age.

Although there were significant weaknesses in this study (which are discussed therein), it remains only the second and most methodologically sound study of its kind. Moreover, both showed the same trends. A key strength of a case-control study such as this one is that it can be a powerful hypothesis-generating tool for subsequent studies. Even though it cannot address causality, it can show strong associations, here between early treatment intervention and avoidance of long-term behavioural problems which have broadly been associated with un-resolved infant colic.

A well-designed prospective study should be undertaken to determine whether these results are spurious or real. This is another area where subgrouping could differentiate between infants within whom regulatory problems are transient versus those who develop long-term behavioural problems.

## Chapter 11. Summary of Study Findings

This chapter links the findings of the research studies within this thesis and suggests implications of the work, discusses levels of evidence and proposes further questions. Table 7 reviews each study's research questions, the findings and follow-on questions. In short, these studies found evidence for the safety and tolerability of chiropractic care for excessively crying infants, the willingness of parents to bring their child for treatment, along with a willingness to pay for that treatment, statistically significant results that the treatment is efficacious in the short-term as well as having some durable utility. These findings may be clinically significant as they make a difference to the patient, families and may lend some guidance to clinicians managing such cases.

Publication	Research Questions	Relevant findings	Questions for further discussion
I. Demographic survey of paediatric patients presenting to a chiropractic teaching clinic.	What is the demographic profile of the paediatric patient attending a university affiliated chiropractic teaching clinic on the south coast of England?	<ul style="list-style-type: none"> <li>*21% of the clinic population were paediatric patients (aged 0-16 years)</li> <li>*62% were &lt;12 weeks of age</li> <li>*78% &lt; one year of age</li> <li>*ECI was most common complaint &lt;12 weeks</li> <li>*MSK complaints were most common over-all, comprising all complaints &gt;5 years of age</li> <li>*All had consulted GP and 43% were taking one or more medications</li> <li>*83% were referred by a medical practitioner, the majority of whom were</li> </ul>	<ul style="list-style-type: none"> <li>How does the demographic profile differ in other non-university affiliated chiropractic clinics?</li> <li>Why (beyond referral patterns) do parents commonly choose this type of therapy?</li> <li>Are parents aware of musculoskeletal problems in their child prior to presentation?</li> <li>Why are younger infants likely referred more than older children?</li> <li>Why do parents who have never experienced chiropractic care (70% of this population) bring their child?</li> <li>Is having had previous</li> </ul>

		<12weeks old infants	chiropractic treatment a deterrent to parental referral?
III. Adverse effects of spinal manipulative therapy in children younger than 3 years: a retrospective study in a chiropractic teaching clinic.	In an audit of a large number of infants and young children receiving chiropractic care, what is the incidence of negative side effects related to chiropractic manual therapy?	*697 children under 3 years of age had 5,242 treatments with no adverse events and a low (<1%) rate of side-effects. The side-effects were mild increased irritability which resolved in less than 24 hours and required no additional medical care or treatment.	*Other studies say that adverse events are under-reported. Is it feasible that parents stand by and not complain if their child were hurt?  *The last reported episodes of adverse effects in paediatric patients were more 20 years ago; has the profession improved management of children in that time frame?
IV. Improving our understanding of the irritable infant: an observational study in a teaching clinic	Which symptoms are more representative of excessive crying most commonly called infant colic?	*Risks for colic include: child appears in pain, inconsolable, flexes legs, changes from happy to screaming instantly, wants frequent cuddling and in families with atopic history	Does this study move us toward subgrouping the inconsolable crying baby?  Do these symptoms give true characteristics of the inconsolable crying infant?
V. QUIC: Initial validation of an instrument to measure infant crying	Can a one page outcome instrument be validated for use with the excessively crying infant?	*There was concurrent validity with the crying diary for amount of infant irritability, distress level, total crying, night-time crying and inconsolability.  A side-effect of care, reported in this study	Is improved sleep a side effect of chiropractic care?  Maternal stress may be related to intensity and soothability of crying, not just any crying activity. Can a study be designed to investigate the

		was a mean lessening of daily crying of 1 hour and 43 minutes by day 7 and a mean increase in night sleep of 29 minutes.	relationship between type of crying and maternal stress?
VI. Prognostic significance of subgroup classification of infant patients with crying disorders: a prospective cohort study	Can excessively crying infants be sub-grouped according to clinical characteristics other than crying time?	Three groups were identified relative to <i>a priori</i> baselines and outcomes of care: 1. Infant colic (IC) 2. Irritable infant syndrome of musculoskeletal origin (IISMO) 3. Irritable feeding crying infant with disordered sleep (IFCIDS)	Since baseline feature of time of crying was undifferentiated, is time of crying a utilitarian way to categorise excessive cry babies?  Study provides support for more robust ways to subgroup excessively crying infants. Is it possible that previous studies of infant colic may not have exclusively recruited colic babies? Babies showed improved sleep and less crying over the treatment time and mothers reported reduced stress levels, although the cohort design does not prove efficacy. Is improved sleep a side-effect of CMT? Is improved sleep related to maternal stress reduction or vice versa?
VII. Efficacy of chiropractic manual therapy in infant colic: a pragmatic single-blind,	1) In colicky infants, is there a difference in crying time between infants who receive	1) Infants who receive chiropractic treatment cry significantly less than those who do not.	This study shows that two different methods of study (blinding and non-blinding of parent) give the same result. Does this finding strengthen

randomised controlled trial	CMT and those who do not?  2) In colicky infants, is there a difference in infant crying time between parents blinded and parents not blinded during treatment?	2) No, there is no significant difference in crying time between babies receiving CMT with parent blinded versus those receiving CMT with parent unblinded.  This study corroborates all of those that previously showed colicky infants cry less with chiropractic treatment.	the probability that the result is correct and can be relied upon? This trial showed that parents leave care after one week if treatment does not work for their child. Can this finding be corroborated in other studies?
VIII. Long term effects of infant colic: a survey comparison of chiropractic treatments and non-treatment groups	Is there a difference in behaviours in children who receive chiropractic care for infant colic versus control group who had colic during infancy but received no chiropractic care?	Control group children were twice as likely to have temper tantrums than those in the intervention group. The intervention group was twice as likely to sleep through the night as the control group and 1.5 times more likely to fall asleep within 20 minutes.	This study found that long-term risks for children with infant colic were significantly less likely if successful treatment had been undertaken during infancy. Can this be corroborated in other studies in order to reduce documented long-term risks from ECI?
CMT – chiropractic manual therapy; ECI – excessively crying infant; MSK –musculoskeletal; OSD – occipital-sacral decompression; ANS – autonomic nervous system; IC – infant colic; IFCIDS – irritable feeding crying infants with disordered sleep syndrome; IISMO – irritable infant syndrome of musculoskeletal origin; QUIC – questionnaire for unexplained infant crying			

**Table 7: Findings of publications I-VIII and implication for further study**

**What are the implications of this body of work?**

These eight studies employed different methods, each chosen to answer specific clinical research questions relevant to the understanding of the excessively crying infant (Table 7). Despite decades of research, there are few answers to the common clinical problem of the

infant who is presented to the clinician with excessive crying. The focus of the research in this thesis was to aid understanding of the problem and the role chiropractic manual therapy might have in its amelioration. Table 8 shows findings in the research studies that were not specific to the research questions but were serendipitous, along with some consolidation and corroboration of results between studies. As such, there are several implications which may spur additional research.

Medical clinicians referred most infants who presented to the chiropractic clinic who were infants, and referred mostly young infants (<12 weeks of age), with the complaint of excessive crying. The younger the child, the more likely the medical referral (studies I, VI, VII).

Most (70%) parents who brought their child for treatment had no prior experience of chiropractic care (study I).

Infants with inconsolable crying have an evening peak of crying (studies II, IV, V, VI, VII).

Infants with excessive crying are different from infants with inconsolable crying (studies IV, VI).

Infants with infant colic should not be defined as having strictly gastro-intestinal symptoms (studies I, IV, VI).

Parents of infants who had chiropractic treatment reported less crying and more sleep after one week of treatment (studies II, V, VI, VII).

Negative side-effects were very low (<1%) and adverse events did not occur with chiropractic treatment for infants (studies II, III, V, VI, VII).

Report of maternal stress decreased with decrease in inconsolable infant crying (studies V, VI, VII).

Parents whose infants did not improve left care after approximately one week (studies V, VI, VII).

The risk of long-term problems may be reduced in children who received successful chiropractic treatment for infant colic (study VIII) and the effect of care for infant colic is intact at least one month post-treatment (study II).

There is evidence of association between inconsolable crying and sleep problems of infancy (studies II, IV, V, VI).

**Table 8: Additional findings to research questions in studies I-VIII**

Although it may be presumptive to apply levels of evidence to one's own research, it seems necessary to attach levels of utility to the findings and conclusions from these studies as a

starting point for further discussion. Of course there are well-defined and accepted evaluation and categorisation systems of evidence where the evidence becomes more persuasive relative to design (Sackett et al., 1996). It is not necessarily appropriate to apply those here as they rely mainly on a hierarchy established by the research method, with systematic reviews at the top and expert opinion at the bottom. With this system, it is a simple matter to say there is only one study in this series which has a relatively high level of evidence, the RCT. This randomised controlled trial was one of only six entered into a Cochrane systematic review and meta-analysis of the highest level types of research done on infant colic to date (Dobson, 2012). The Cochrane Library is a respected source of reliable evidence as it relates to health care. In their 2012 Cochrane review of infant colic, over 300 potential studies were surveyed and only six were included. Further, they cited this particular work for special commendation due to its novel approach to test both the blinding and the therapeutics effectively in the same study.

However, strong evidence is not always the most clinically applicable or meaningful (Manchikanti et al., 2009). One purported goal of evidence based practice is to provide the best answer to a clinical question in a timely fashion. These studies have clinical utility now, but may not withstand the test of time and may be super-ceded by more and higher quality evidence as it occurs. However, I propose that at this time, the findings of this study series go some way to answer some clinical questions, with various levels of support. I suggest using the following terms:

- significant support if the findings are backed by a RCT and 3 or more studies in the series
- moderate support if the findings are backed by 3 or more observational studies in the series
- mild support or trends that were found in at least 2 studies in the series

From these studies, significant support was found for the following conclusions:

- 1) Infants with a condition commonly called infant colic cry significantly less after a short course of chiropractic treatment.
- 2) Significant reductions in inconsolable crying occur whether the parents are blinded to treatment or not, thus adding strength to the result.
- 3) A large cohort of infants with excessive crying were sent by medical practitioners and brought to the clinic by their parents, willing to pay for treatment.
- 4) Infants with inconsolable crying demonstrate an evening peak of crying.
- 5) Chiropractic manual therapy is safe for infants.

From these studies, moderate support was found for the following conclusions:

- 1) Mothers report improved infant sleep after a short course of chiropractic treatment for the child.
- 2) Mothers of infants report significantly less stress when the child's crying improves.
- 3) The types of excessive crying are not all the same; some have different aetiologies and a unique clinical course.
- 4) Outcomes can be accurately measured with a one-page instrument rather than relying solely upon the cumbersome crying diary.
- 5) Infant colic is not strictly related to the gastro-intestinal system and should be re-named.

From these studies, mild support or trends were found for the following conclusions:

- 1) Medical clinicians are aware of the potential of chiropractic manual therapy to help inconsolable crying of infancy.
- 2) Parents are aware of musculoskeletal problems of children and present their child to an appropriate practitioner and nearly always check with their medical clinician first.
- 3) There may be a biomechanical component related to excessive crying of infancy and this may be the case in both inconsolable crying and excessive crying. There may be an autonomic nervous system component of some types of excessive crying.
- 4) There may be long-term benefits for the child who has had chiropractic manual therapy for inconsolable nocturnal crying of infancy.

Perhaps other researchers will design higher quality studies to put these concepts and theoretical ideas to further testing.

### **Toward a more utilitarian name**

The findings of these studies support a change in the naming of infant colic. The reason to propose a name change is that the term, infant colic, presupposes that colic, or digestive disturbance is implicated by definition (Dorland's Medical Dictionary 2007;p389):

*"Pertaining to the colon. Acute abdominal pain; characteristically, intermittent visceral pain with fluctuations corresponding to smooth muscle peristalsis."*

For some time, there has been considerable evidence accrued that the malady called infant colic has nothing to do with "colic" or irritation to the digestive system, showing no differences between colic and non-colic babies (Yalcin et al., 2010). In fact, x-rays showed there was less gas at institution of crying than at the end (Illingsworth, 1985). For many years, the condition was defined in terms of time of crying, rather than according to any specific symptoms (Wessell et al., 1954). The hallmark of infant colic is not merely

excessive crying (which occurs in other conditions as well), but inconsolable crying concentrated at one time of the day, most commonly late afternoon, evening to night-time. Infant colic (IC) has an evening peak, is known for its inconsolability and it is suggested herein that it might be termed inconsolable nocturnal crying syndrome (INCS). Table 9 gives defining features of different types of or reasons for infant crying.

<b>Current term for infant crying</b>	<b>Defining features</b>	<b>What consoles infant</b>	<b>Descriptive name for type of crying</b>
Infant colic	Evening cluster, cannot be consoled	Nothing during crying episodes	<b>Proposed:</b> <i>Inconsolable nocturnal crying syndrome</i>
Irritable infant syndrome of musculoskeletal origin	Postural cluster of crying	Antalgic posture	Irritable infant syndrome of musculoskeletal origin
Kinematic imbalance of suboccipital strain	Postural cluster of crying	Cervical extension	Kinematic imbalance suboccipital strain
Cow Milk Protein Allergy	Feeding cluster, worse after feeds	Change to hypo-allergenic feed	Cow Milk Protein Allergy
Irritable feeding crying infant with disordered sleep syndrome	Short fuse, starts crying, cannot stop	Nothing predictable, erratic, rarely happy, parental attempts futile	Irritable feeding crying infant with disordered sleep syndrome
Urinary tract infection or other painful illness	Systemic features	Correct treatment for the problem	Well child when treated for disorder

**Table 9: Defining features of types of excessive infant crying and their names**

Infant crying should only be called excessive when the reason(s) for the crying are unknown. For example, crying related to a painful urinary tract infection should not be labelled as excessive crying. Once the reason is found and treated, the crying abates. The same is true for crying related to cow milk protein intolerance. Once understood and treated with the appropriate feed, then the crying subsides. Excessive crying should only be

termed so when the amount, extent and intensity of crying cannot be understood by the parent or clinician and that the amount of crying is dysfunctional for that baby. This underlines the fact that all infants should be examined for any type of occult injury (Freedman et al., 2009), pathology, infection or problem that results in a context-specific cause of the crying before being termed an excessively crying or irritable infant with no known cause.

Inconsolable nocturnal crying syndrome reasonably describes the concept of infant colic and excludes the misnomer of connection to the infant's colon. If the term infant colic cannot be extinguished, then we should consider using it as an acronym; for example the term COLIC could then represent a more descriptive, if cumbersome, expression such as Cause Obscure Lengthy Infant Crying (COLIC).

### **Strengths and Limitations**

The strengths and weaknesses of each study included within the publications in this thesis have been illuminated in the introduction to each study and within each publication. There are, in addition, over-all strengths and limitations of the integration of these studies.

This body of work offers the newest and highest levels of research into the chiropractic care of infant colic, and as such, it has moved the body of knowledge forward. This remains the largest, most cohesive and advanced series of studies in this area to date.

A strength of this series is its potential wider application to fellow professions such as osteopathy and physiotherapy. However, the relevance of these studies is not limited to these professions; it is also relevant to the condition itself and researchers from all professions interested in the infant may be able to utilise findings of this research to further investigate aetiology and sub-grouping of patients. One of the papers was invited for presentation at the Royal College of Paediatrics and Child Health annual meeting (Miller et al., 2012), which suggests a possible wider interest in this body of work. Another paper (Green and Miller, 2007) was invited for presentation at the Exeter University 2007 Complementary and Alternative Medicine (CAM) conference. These methods of data collection have been adopted by other researchers (Arnesen, 2013; Kelly, 2013) and the proposed sub-grouping has been used in other studies or protocols for other studies (Alcantara and Anderson, 2010; Arnesen, 2013; Dobson 2013).

This thesis corroborated, in infants, what has been learned in adult studies of chiropractic care, that most subjects improve rapidly from the first treatment onward (Hestbaek et al.,

2003; Pengel et al., 2003). This concept may be helpful to clinicians to determine, early on, whether they are “winning or losing a case,” and could help in appropriate and ethical clinical decision-making regarding length and number of treatments in an episode of care.

Further, this thesis goes some way toward filling a gap in the research literature regarding the relevance of musculoskeletal health, chiropractic manual therapy and infant colic. In that sense, there may be justification for the potential link between infant colic and musculoskeletal health of the infant, in that the similarities between infant colic and back pain (where musculoskeletal health issues have been established) are considerable (Table 10).

<ul style="list-style-type: none"> <li>• Both are costly benign conditions in society.</li> </ul>
<ul style="list-style-type: none"> <li>• Both are common reasons for health care consultation in their age groups.</li> </ul>
<ul style="list-style-type: none"> <li>• Both have a rare aetiology in pathology, less than 5%.</li> </ul>
<ul style="list-style-type: none"> <li>• Both are difficult to specifically diagnose.</li> </ul>
<ul style="list-style-type: none"> <li>• Both have associations with often called “trivial” trauma that preceded the incident.</li> </ul>
<ul style="list-style-type: none"> <li>• Both have an enormous impact on families, society and health care, with bio-psycho-social negative sequelae causing problems with activities of daily living of the patient as well as the family.</li> </ul>
<ul style="list-style-type: none"> <li>• Both have high rates of chronicity (more than 50% in infant colic and up to 80% in back pain).</li> </ul>
<ul style="list-style-type: none"> <li>• If the conditions become chronic, they are associated with long-term negative sequelae including depression and change in work habits in the adult and aspects of neurodevelopment in the infant, both suggesting links to the cumulative effects of pain and stress.</li> </ul>
<ul style="list-style-type: none"> <li>• Both are otherwise healthy.</li> </ul>
<ul style="list-style-type: none"> <li>• Both show some beneficial outcomes with chiropractic manual therapy.</li> </ul>
<p>Source: American College of Physicians and the American Pain Society, 2007; Dobson et al., 2013; Erlich 2003; Freburger et al., 2009; Freedman et al., 2009; Hemmi et al., 2011; Hoy et al., 2010; Keefe et al., 1999; Kent and Keating, 2005; Morris et al., 2001; WHO, 2010; Zwart et al., 2007.</p>

**Table 10: Similarities in low back pain in adults and excessive crying of infancy**

Study VII, a randomised controlled trial, could be considered at least partly generalizable to the wider population and was used in a meta-analysis and a Cochrane review of manual therapy for infant colic (Dobson et al., 2012). Generalizability is the goal of research in order to move the knowledge base forward. RCTs, such as this one, can provide a basis for further study and one such additional RCT is now in the planning stages (Dobson, 2013).

There are many limitations to this work. As a group, this series of studies is essentially, too little and too late and weak in the hierarchy of evidence. There is such a deficit in the total body of related literature that this series makes but a tiny contribution to the over-all requirements of research in the field of manual medicine for infants suffering from excessive crying. To consider generalizability from any study except the RCT is premature at best, and impossible in the least.

A key limitation to all of the studies is that the population studied are those that presented to a chiropractic teaching clinic, most commonly referred from GPs, midwives or health visitors. This alone indicates that the subjects are likely to be different from the general population. First, users of CAM have been noted to have more education than the general population (Mootz et al., 1997). Further, since most of the patients within these studies were referred for care, their health status may have been more severe, or otherwise unique from the wider population. The parents of the subjects must have been receptive to attending the clinic and by and large, were able to pay for it. This is a clinic outside of conventional health care in the UK, where the National Health Service manages the greatest proportion of all health care needs of the population. It is possible that there is only a certain socio-economic strata represented in this subset of patients. It should, however, be noted that this clinic provides care at relatively lowered fees from private clinics and that care is never denied due to inability to pay. Fees most likely matter in the arena of health care and this requires careful consideration in the generalizability of these studies. Further, these parents may be seen to have advantages that others don't have regarding choices of treatment and further study into the socio-economic status and course of infant colic are indicated to clarify these issues.

Further, these studies comprised patients seen only in this college-affiliated chiropractic teaching clinic, which is unlike most venues where similar types of care might be offered. It is unknown whether the care offered therein is unique to this clinic or similar to others. That said, since it is a teaching clinic, it is likely to lead the types of care offered and these would possibly be reproduced in the field as students graduate. That said, education is only part of clinical expertise and there are likely to be variations in the care given by diverse practitioners, no matter where they received their education. Also, manual therapy is not unique to a single profession and it may be thought that the outcomes from the type of care in a chiropractic clinic may be applied to the practices of osteopaths or physiotherapists. More evidence would need to be gathered to determine whether or not

there is generalizability across professions. The Cochrane collaboration thought the data was generalizable and it included all types of manual therapy in a meta-analysis of manual therapy for infant colic (Dobson et al., 2012). Whether or not that is an appropriate assumption remains to be investigated.

The services of this clinic are novel, as well, as they are provided by students overseen by faculty, which is unusual within the area of patient care. The students may have much less expertise than the average private practitioner; on the other hand, the faculty may have more experience than the average clinician in private practice. No matter how it is viewed, there are significant differences between this clinic and that of the average private practicing chiropractor. The results may not be generalizable due to significant differences in other countries, as well, since this clinic sits on the south coast of England with a specific socio-cultural milieu that is likely different from other parts of the world.

### Personal reflections

This thesis presents an elaborative analysis of research spanning more than a decade into the relevance of chiropractic manual therapy to excessive crying in infancy through a unique series of eight clinical investigations. The overall purpose was to address a paucity of research into the appropriateness of manual therapy for this condition, especially in its diagnosis and management, and also to investigate linkages between infant pain and musculoskeletal health. What instigated this study were significant gaps found in the research. The novel research included in this thesis has moved the knowledge base forward to help close those gaps. This thesis provides answers to questions of both aetiology and management. This is not to imply that these are the final or even the only answers. With such a complex condition, there are likely to be complex aetiologies. This thesis begins to fill some of the major gaps and helps reassure both parents and clinicians that manual therapy for excessive crying is safe and potentially beneficial for many infants. With a NNT (number needed to treat) of 3, chiropractic manual therapy can be considered a very useful treatment. With the primary aim of this research to improve health and patient care, this NNT indicates a strong benefit for the infant undergoing chiropractic management for infant colic.

There is also benefit for the professionals who provide manual therapy for infants in that they have a guideline on which to build their expectations and a method of treatment which has shown significant efficacy. It is unknown whether this equally applies to

chiropractors, osteopaths and physiotherapists, but the Cochrane research group applied my innovative research to all of the professions providing this type of care. The key here is that the types of treatment used throughout the studies in this thesis were entirely controlled low force (approximately 2 newtons or less) and that higher forces are unnecessary and contra-indicated for this age group. This has been covered well elsewhere, but was corroborated in my research studies.

Doing this research has made me keenly aware of the importance of ethical practice in research including complete anonymity and well as autonomy and self-decision-making for the parents. The breadth of studies undertaken in the process of this thesis has raised my awareness of the need for more research and the importance of using the most appropriate methodology to answer the research questions.

The findings from this thesis resulted in a model whereby the mechanical forces of labour and birth could cause a biomechanical disturbance to sensitive tissues in the infant which might instigate unsettled behaviour maintained by hypersensitivity of the central nervous system. This concept is corroborated by other research that has shown that the cumulative effects of pain and stress in the infant, when not alleviated, may continue to compromise the neurodevelopment of the system resulting in poorly adapted internalising and externalising behaviours. This concept was further supported by the case-controlled studies in this thesis that showed that treatment, when effective, seems to stem this tide. Since a musculoskeletal therapy treats the condition successfully, it can be considered a fairly strong indication that a musculoskeletal component is at least partly responsible for the aetiology of the condition. Therefore, what this series of my studies brings to the table is at least a small amount of needed clarity to see excessive crying of infancy through the lens of musculoskeletal care. This is a novel approach which requires more study and it strongly indicates the relevance of a small community demonstration project to determine whether these benefits hold true in a wider community setting. My thesis demonstrated the following contributions to the knowledge base never previously put forward:

- First time to subgroup crying babies and first time to find significance in the groupings;
- First time to create an objective outcome measure and validate against the crying diary;
- First time to test parent blinding;

- First time to demonstrate that chiropractic manual therapy was effective for infant colic against a blinded non-treatment group;
- Proposed a new definition of excessive infant crying not based on crying time, but other parameters (maternal report and statistical significance);
- First time to demonstrate strong inter-disciplinary connections with high referral rates of infant patients from medical care to chiropractic care;
- First time to develop a predictive model using likelihood ratios to forecast the presence of infant colic in a clinical population.

This thesis also demonstrated the importance of using more precise definitions of the excessively crying infant. The ability to define excessive crying in terms of other parameters instead of crying time helps to alleviate one of the main controversies namely that the crying time in research trials may be too close to the referenced norm to have significant research or clinical utility. Having other ways to define the syndrome may allow better or at least alternative ways to assure that the infants under study are the same and not widely different in their characteristics. This could serve to improve the quality of future studies. This is, likewise, a strong benefit of the sub-grouping demonstrated in this thesis. This may go some way to develop and improve pathways for inclusion and exclusion criteria for research studies to more closely identify the characteristics of the infants under study. There is no longer a need for infant colic to be either a diagnosis of exclusion or a wastebasket diagnosis. There are ways demonstrated in this thesis to identify these infants and separate them into categories. This will certainly be refined and improved in future studies.

My hopes for this work are to provide some much-needed clarity of direction, to reduce fragmentation of care which has long characterised the management of infant colic and to promote inter-disciplinary research to improve the lives of afflicted infants and their families. The information provided in this thesis can help decision-makers (whether in the family, the clinical setting or community) view additional options for care. These are improvements over the most common current option of doing nothing, which has been shown by this evidence to be a less effective choice than chiropractic management for infant colic.

## **Chapter 12. Proposal for assessment, mechanism and cost-effectiveness of manual therapy for infant crying syndromes**

The purpose of this chapter is to answer some of the issues which arose from the eight research studies comprising this thesis. The aims of this chapter are to:

- A. discuss the arguments for and against a rationale for early musculoskeletal assessment of the neonate;
- B. propose a plausible mechanism of chiropractic manual therapy for the inconsolable infant;
- C. examine a cost comparison of chiropractic treatment with routine treatment for excessive crying of infancy.

Chiropractors are not only in the business of treating musculoskeletal maladies, but also preventing them. If inconsolable nocturnal crying of infancy can be treated successfully with chiropractic therapy, the question must be asked whether an early musculoskeletal examination might prevent it. Beyond these findings, is there sound rationale for an evidence-based model for early assessment of the healthy newborn?

### **A. Should infants undergo early musculoskeletal assessment?**

Musculoskeletal irritation and injury is common at all ages. Birth injury, unless major and life threatening is under-recognised and under-treated (Gottlieb, 1993). Birth, even under normal conditions, consists of significant traction and rotation of the baby's head, with sufficient force to cause clavicle fracture, but is known as "an unavoidable side effect of birth" in up to 10% of vaginal births (Mavrogenis et al., 2011). Birth injuries are more common with more assistance. Forceps deliveries are associated with skull fractures, cranial nerve palsies, brachial plexus injuries, facial nerve injuries and torticollis (Ritzman, 2004). Cephalohaematomas and cranial fractures are associated with Ventouse delivery (O'Mahoney et al., 2010). Vacuum extraction has been shown to be a strong predictor of early cessation of breast feeding due to injury (Hall et al., 2002). It is increasingly common for births to be assisted with vacuum extraction equipment or surgery (Kozak and Weeks, 2002). In a recent study of 200 children presenting to a chiropractic clinic with pain and other physiologic disturbance, 95% demonstrated notable birth trauma (Edwards et al., 2010). In a much earlier (Frymann, 1966) and larger medical study of 1250 newborns, 89% showed some mechanical strain or restriction

Birth injuries are shown in Table 11. The list of mild injuries are those which would likely be detected by a musculoskeletal assessment. The list of moderate and severe injuries would likely be detected with the current early examination which, in the UK, occurs within 72

hours of birth and includes a screen for eyes, heart, hips and testicles (NHS, 2012). However, musculoskeletal injuries are not always detected and Joseph and Rosenfeld (1990) stated that the frequency of fractures diagnosed in the first assessment is significantly under-estimated. Medical clinicians may not feel comfortable with diagnosis and treatment of musculoskeletal injuries in childhood (Jandial et al., 2009; Gill and Sharif, 2012). One chiropractor in Norway (Monson, 2013) found 16 cases of undetected clavicle fractures from birth in a single practice. Forty-six rib fractures, occurring from but undetected at birth in 13 cases, have been reported in the literature (Van Rijn et al., 2009).

Another over-looked birth injury is torticollis. Torticollis is wry neck resulting in distorted use of the head due to an inability to utilise full cervical spine range of motion, almost always declared a birth injury at the neonatal stage (Cheng and Au, 1994). The incidence rate has been reported as being between 1.2-3.92% (Cheng and Au, 1994; Chen et al., 2005). A more recent (Stellwagon et al., 2008) study found a much higher rate of 16% and suggested that this condition is frequently missed due to incomplete musculoskeletal examination. It seems logical that the general examination in hospitals is focused on severe (life-threatening) types of trauma and mild or moderate injuries may be over-looked.

Mild Injury	Moderate Injury	Severe Injury
Asymmetry of the head 61% [1] Facial asymmetry 42% [1] Torticollis 16% [1] Asymmetry of the mandible 13% [1] Nasal septum deviation 0.93% [2]	Clavicle fracture 0.4-10% [3] Facial Nerve injury 0.75% [4] Bruising and tearing of spinal nerve roots 0.3% [5] Brachial Plexus 0.11-0.26% [4], [6]	Extra-and subdural haemorrhage into joint-capsules and torn ligaments and dura 0.96% [5] Haemorrhages of vertebral arteries 0.85% [5]
[1] Stellwagen et al., 2008; [2] Podoshin et al., 1991; [3] Mavrogenis et al., 2011; [4] Levine et al., 1984; [5] Yates 1959; [6] Perlow et al., 1996		

**Table 11 Neonatal birth injuries categorized by severity**

At increased risks of musculoskeletal injury is the male child born to prima para mothers using assisted methods (Levine et al., 1984; Torvaldson et al., 2006). It is also particularly the case that these infants are at greater risk of replacement feeding if the new mother and

baby cannot manage breastfeeding (Hall et al., 2002; Smith, 2007). Breastfeeding is the healthiest option lifelong (World Health Organization, 2010) and it may be easily compromised after a difficult birth, not least because of drugs employed that may affect the newborn but also musculoskeletal injuries about the head and face. However, mothers and newborns may not get the help they need. One in four women is critical of the routine post-natal care and feeding support they received (Bick and Bastos, 2012). Since babies with mild injuries have a high rate of cessation of breastfeeding (Wall and Glass, 2006), manual support may be helpful to restore biomechanical function. One study (Miller et al., 2009) showed that 79% of new mothers presenting for feeding problems were able to exclusively breastfeed after a short episode of chiropractic treatment. If these problems could be found *before* breastfeeding cessation occurs, a great deal of anxiety might be avoided, as well as trips to the hospital for common sequelae of poor feeding such as dehydration (Wall and Glass, 2006).

If early detection of birth injury is a benefit, what are the risks of early musculoskeletal assessment? The assessment is non-invasive, done only by hand without instrumentation and performed completely within the family unit, displaying less force than a mother might employ with a pat on the back to aid digestion or wind the baby (Hawk et al., 2009). Early examination provides an opportunity for treatment before dysfunction begins. There are no reports in the literature of any injury due to chiropractic examination of the infant or child (Humphreys, 2010).

The converse question also must be asked. What are the risks of not doing a musculoskeletal screen? Are there any short or long-term risks of unnoticed spinal or muscular distortion or fractures, for example, in the clavicles or ribs? Damage does not occur exclusively to physical tissues but also to neural programmes that control movement patterns, protective postures and general alignment. That is why early treatment is recommended, to work within the critical window before unused synapses are pruned and correct neural patterns. It can be said that the earlier that a basic skill is learned, the longer the consequences of its malformation. Any maladaptation can derail kinesiological development long-term or require much more extensive treatment later. This is why even minor signs of postural aberration should be treated (Miller and Clarens, 2000).

Asymmetry alone may not cause problems but may predispose the child to difficulty in adapting to normal physical movement or to adopt movement errors. Functional problems

of childhood will become hardwired in the nervous system if they are not ameliorated (Biedermann, 1995).

Further, there are known risks associated with the excessively crying infant such as shaken baby syndrome (Carbaugh 2004) and insecure infant attachment (Taylor et al., 2005). In cases where excessive crying occurs due to occult birth injury, then those risks may be avoided through early detection and treatment. As a chiropractor may be able to detect and treat mechanical problems of the excessively crying infant (Miller et al., 2012), there may be potential for an assessment to take place soon after birth, before the excessive crying begins in earnest. It is documented (Jandial et al., 2009; Gill and Sharif 2012) that paediatricians and other non-MSK specialists have a low estimation of their own ability to manage musculoskeletal cases. The chiropractor's expertise is in the exact area where other clinicians have little and it is reasonable to recommend musculoskeletal expertise for musculoskeletal maladies (Murphy et al., 2011; Foster et al., 2012).

Saying that children do not have musculoskeletal dysfunctions could be viewed as age discrimination. Stating that children do not require care for their musculoskeletal disadvantages is to remain blind to the long-term consequences that musculoskeletal disability has on health. The benefits of early assessment require evidence. Therefore, cohort or other types of studies should be undertaken to investigate whether infants who have intervention sustain any lower risk for complaints of excessive crying or other maladies of infancy or toddlers. One study (Miller and Phillips, 2009) in this series suggests long-term benefits.

Prevention is preferred to treatment. But when treatment is needed, manual therapy has shown promise of effectiveness (Mercer and Nook 1999; Wiberg et al. 1999; Karpelowsky 2004; Koonin 2005; Hayden and Mullinger 2006; Miller et al., 2012) for excessive crying. The question remains as to the plausible mechanism of such treatment techniques.

### **B.Plausibility and mechanism of chiropractic manual treatment for the newborn and infant.**

If a musculoskeletal examination is in order, then musculoskeletal treatment may be appropriate. This is where the problem lies because the infant cannot say, "it hurts here." That said, even in adults, determining the exact source of pain can be difficult due to referred mimicked pain (Murphy and Hurwitz 2007). For example, it is well known that gall bladder pain refers to the shoulder but through active and passive movement and

orthopaedic tests, it is usually possible for the clinician to determine whether the origin of the pain is local (in the shoulder and biomechanical) or distant (gall bladder and pathological) (Slaven and Mathers, 2010).

None of this precision is possible with the infant, who may not be able to recognise pain for what it is (Chapter 1). Nor can they point to it or undergo testing procedures to discriminate the cause of pain (as muscle tests require resistance, which the infant cannot comprehend or provide of their own volition). Consider that the child will usually cry with pain; in some cases, crying may make the pain worse and the child may discontinue crying after some time, but show other types of pain behaviour, such as antalgic posture. If the caregiver is not observant, the signs of discomfort may be missed.

### **1.Importance of posture and position in health**

Although postural preferences in newborns have been the subject of study for some time (Casaer, 1979), whether these should be treated has been questioned (Rosenbaum, 2006). However, when left untreated there is evidence (Binder, 1987; Cioni et al., 1989; Boere-BooneKamp and van der Linden-Kuiper, 2001; Philiippi et al., 2006) of long-term persistence of postural asymmetries in up to 50% of cases and this is why researchers and clinicians highlighted the importance of therapeutic procedures even in early years of life. Postural fault concentrates stress locally, which sooner or later, may cause pain, discomfort or further dysfunction.

Postural medicine studies the effects of position and gravity on the human body (Martin-Du Pau et al., 2004). For example, a patient with disc disease generally has more pain while seated. Sudden Infant Death Syndrome (SIDS) is more common in prone sleepers while gastro-esophageal reflux disease may be alleviated by sitting upright (AAP, 1992).

Just as architects take into account the laws of gravity and weight distribution to increase resistance to stress and strains in a building under construction, the human body requires good alignment with a straight (uncurved) spine balanced over the lower limbs in order to distribute the weight evenly over discs, ligaments and joints. Oddly, these principles are often over-looked in young infants, possibly because they do not stand upright. To redress this oversight, Nuysink and colleagues in 2011 proposed a screening instrument to detect symptomatic asymmetries of head position in young infants since infant positioning has been the focus of the Back-To-Sleep campaign recommended by the American Academy of Pediatrics (1992) task force on infant positioning.

Chiropractors seek to prevent disability by directing care toward good postural alignment as well as treating mild joint dysfunction which can lower the threshold to pain. The lowered threshold to pain is called sensitisation. This has been shown (Hermann et al., 2006) to occur in newborns with difficult births and to be maintained in the system through to adolescence (Lidow 2002). Sensitised nociceptors can discharge spontaneously with any innocuous movement or gentle touch (Seaman and Cleveland, 1999). It is logical to suppose that children become more comfortable when the cause of their skewed posture is found and treated through re-alignment of the joints. A more balanced posture is accompanied by a cessation in pain behaviours (antalgic posture and crying).

## **2. Manual treatment to reduce pain**

Studies in animals and adults have described a mechanism of chiropractic manual treatment as related to the gapping of zygapophysial joints, thus breaking adhesions which develop with hypomobility and stiffness of joints (Colloca et al., 2004). Pandiculation is a rigidity from hypomobility, a tendency of early stage stiffness documented in infancy (Philippi et al., 2006). This is further suggestion that musculoskeletal disorders that plague adults start early as the presence of musculoskeletal imbalance at birth has been documented (Wall and Glass, 2006; Stellwagon et al, 2008).

Joint hypomobility is seen in infancy and is a logical sequelae to mild spinal trauma during birth, or relative lack of mobility during the crowded last weeks of gestation. Chiropractic treatment (gapping of the joints) in this age group consists of positional therapeutics (such as stretching or decompression) or “press and hold” soft tissue techniques as there are no thrusts presented to the young spine and most of the force is transmitted via soft tissues to the spine, not to the spine directly. Any association of treatment with a “cracking” sound (cavitation) is completely inappropriate for the infant patient. Nowhere is it clearer that infants are NOT small adults and key aspects of care must be reconsidered for the infant patient (Marchand, 2013).

It is plausible that soft tissue work involving light to moderate tactile pressure and muscular stroking techniques might decrease muscular spasms, improve circulation, reduce adhesions, re-align soft-tissues, re-align joints, improve range of motion, increase relaxation and thus alleviate pain or discomfort (National Center for Complementary and

Alternative Medicine, 2007). Research (Smith et al., 1994) shows that therapeutic massage disrupts the acute inflammatory process, reducing levels of serum creatine kinase and decreasing muscle soreness after extensive eccentric usage of muscles. This type of muscular activity could occur during birth processes, causing injury and pain. Soft tissue manual therapy has been shown to alter pain producing acute inflammation and substance P levels in patients with known soft-tissue pain syndromes (Smith et al, 1994; Field, 2002). Success in doing this has also been shown with specific joint compression and deep tactile distribution of touch-pressure (Farber, 1982).

However, other questions arise as to what mechanism might reduce pain in the child when the mode of onset and mechanical lesion is less clear. Are pain-expressive behaviours due to mechanical lesions when no other source (such as infection, causing systemic markers) can be discerned? Could anything other than restored biomechanical comfort to the infant account for change in behavioural patterns? Is mechanical force simply one potential key to unlock a complex physiological response that results in significant or profound pain modulation through the central nervous system (CNS)? Virtually all adults have experienced aches and pains that can incite lowered patience and “shorten a fuse.”

One of the hallmarks of the inconsolable baby is a hyperactive autonomic nervous system (ANS) (LaGasse et al., 2008) which has two components, the sympathetic and parasympathetic nervous systems (SNS and PNS, respectively). It is reasonable that inconsolable crying is related to a hyperactive sympathetic nervous system (SNS) and this has been described in both baby and caregiver (LaGasse et al., 2008). The cry is like a siren to the parent, an aversive stimulus, which must be turned off. When the cause cannot be found (and thus relieved), the parent becomes as tense as the child. Several studies (Murray, 1979; St. James-Roberts, 1999; Miller and Newell, 2012) have shown correlations between the baby’s inconsolability and the mother’s report of stress. It is likely that these tensions then reinforce each other, creating an increasing imbalance in the autonomic nervous system. Treatment may be required to rebalance the system.

However, it is less easy to discern why a baby with inconsolable crying who is treated with manual therapy immediately stops crying and becomes, in the words of the parent, a “completely changed” and placid baby. Is this a biomechanical physiological structural change response that is too minor to be perceived by the parent or is it a powerful hyperalgesic dampening effect induced by the manipulation? Something in the baby’s

world has shifted. Is this a resetting of the autonomic nervous system? This theory was proposed by Hipperson (2004) and this has been likened to restarting a computer to put its actions back into balance, improving equipoise between inhibition and excitation. Or, does a mechanical force to the painful tissue expedite a reduction in pain mediated by and resulting in a calmed ANS? Most of medicine consists of chemical treatment. Chiropractic manual therapy is mechanical treatment but may involve a release of pain-busting chemicals with joint motion (Bialosky et al., 2009) and these mechanisms are outlined in Table 12.

<p>Target tissues of manual therapy are skeletal system, nervous system and soft tissues.</p> <p>A mechanical force initiates a chain of neurophysiological responses which produce the outcomes.</p> <p>Mechanism of action is mediated by the dorsal horn of the spinal cord and periaqueductal gray zone.</p> <p>Spinal cord responses following MT provide a barrage of input to the CNS (acting as a counter-irritant), documented with fMRI, resulting in a decreased activation of the dorsal horn (and accounting for analgesic effects of MT).</p> <p>A supraspinal response, associated with ANS responses, result in descending inhibition of pain due to associated changes in the opioid system.</p> <p>Significant declines in serum levels of cytokines have been observed after manual therapy.</p>
<p>MT: manual therapy, fMRI = functional Magnetic Resonance Imaging; ANS = autonomic nervous system; CNS = central nervous system. (Bialosky et al., 2009)</p>

**Table 12: Model of mechanism of manual therapy for pain syndromes**

The same general effect is seen with another effective therapy for infant crying. Dicyclomine is a drug that decreases crying in colicky infants, but has been removed from the market because of dangerous side effects (Garrison and Christakis, 2000). Its ability to resolve crying indicates nothing about the cause of the condition as it is a central nerve depressant with side effects of coma and death; thus, its effects are general, not specific to the cause of colic. It appears that changes to the entire system are mediated by the central nervous system, whether these changes are instituted chemically or mechanically. Fortunately, when CNS changes are incited through mechanical stimulation, adverse effects are extremely unlikely. The mechanism of therapy may depend on whether it is a “hardware” or “soft-wear” type of problem. Therefore, two mechanisms are proposed.

### 3. Two proposed mechanisms of manual therapy in infants

Two parallel mechanisms of healing in children with manual therapy are proposed herein. The first is simple biomechanical realignment by skilled hands of joints misaligned by intra-uterine constraint or difficult birth. The second is due to nervous system changes, sometimes working by both biomechanical reconfiguration through relief of near-anatomical irritation along with CNS chemical and neurological pain desensitisation.

First, in some patients, there are biomechanical faults: a shortened muscle through fibrosis; a damaged ligament such as the anterior talo-fibular ligament in a sprained ankle; or a loosened (or frozen) spinal joint caused by a difficult birth process. When these are corrected, it is like screwing the lid onto a jar. When it is aligned correctly, the system works well but when it is misaligned, the cover cannot be replaced tightly and the system never works flawlessly until corrected. Sometimes, mechanical fault is simply a matter of re-alignment and this can be treated instantaneously with almost instant relief for the patient (with some time for healing to take place depending on the time frame of the injury). With good alignment comes improved comfort. This is primarily a local phenomenon.

Second, the human body also works as a complex unit. There are central mechanisms that assist in pain reduction, such as descending inhibitory impulses. However, without joint re-alignment the pain reduction may be only temporary and it may have to be instituted repeatedly until the body adopts a new pain-free or irritant-free status quo. The system resets. This can occur instantaneously or it can take time, over a few sessions, for the system to adapt to the change. Frequent treatment “reminds” the body to maintain appropriate alignment until full recovery or normal elasticity of the tissues ensue. The CNS “resets” through a series of neurological and chemical cascades (Bialosky et al., 2009)

The question remains as to why children recover more quickly than adults. Of course, young tissue heals faster. Also, there is less psychological over-lay in the child and no reason for the child to have sickness behaviour or an aversion to wellness. It is unlikely that there is any attention to positive reinforcement of illness behaviour during infancy. It is more likely that the time it takes to reset the system is not accounted for by hesitance in the psychology of the child but rather time for the system to rebalance or heal after some

time out of equilibrium. The earlier this happens, the less likely the organism is to become sensitised. The earlier it happens, the less time it takes for realignment and the ability to sustain appropriate posture to manifest. The key is to return the child to pain-free full function. The child may then feel better, feed better, sleep better and cry less. When functions improve, their behaviours may tend to improve. It stands to reason that removing the irritant could have long-term as well as short-term benefits

These two mechanisms may help explain why some babies improve instantaneously with one manipulation while others require a series of treatments (on average four) recovering more slowly, but still over a shorter period of time than the known natural history of the disorder (Wolke et al., 2002).

Despite these proposed mechanisms which may successfully treat biomechanical constraint or musculoskeletal dysfunction in the child, still there may be a myriad of reasons as to why babies improve from excessive crying with chiropractic treatment. Table 13 proposes a list of potential reasons; however, these should not be considered exhaustive or exclusive.

- The mechanical treatment redirects the musculoskeletal misalignment and the baby becomes settled due to improved physical comfort.
- The baby's autonomic nervous system is reset, calmed or balanced and the baby is emotionally comfortable.
- Both of the above may work together
- Treatment results in decreased pain through desensitisation of the nervous system.
- The condition is self-limiting and the baby improves (albeit well in advance of the documented age of 5-6 months)
- Regression toward the mean
- Outcome of unknown treatment effects
- Biased reporting of the parent
- Biased reporting of the doctor
- Placebo effect on the baby
- Placebo effect on the parent
- Those who present for chiropractic care are high-responders to treatment and placebo effect and would improve no matter what type of care was given (although it should be explained how they had previously presented to other clinicians and undergone care without success). Randomisation should remove this effect.

Table developed by author

**Table 13: Possible reasons for improvement with chiropractic treatment**

There is continued search for therapies that work for infant colic. Pharmacology has demonstrated no benefits for the excessively crying baby in several double blind studies (Lucasson et al., 2010). Manual skills, which individualise variable palpatory pressures may uncover functional rather than pathological problems in the infant. The final common pathway of manual therapeutics performed on infants is one of release; joint release when immobility is observed and myofascial release when a muscle is tonic. When these are factors preventing normal biomechanical actions in the child, s/he may feel relief with release of the constraints of the tissue.

It is perhaps difficult to contemplate a deviation of care from the well-established medical model with all of its advanced technological capabilities and resources, particularly in dealing with the needs of an infant. There have been mismatches in the interpretation of the biomedical model for example (van Teijlingen, 2005) and he proposes a more critical analysis from a sociological perspective. This is to be broadly supported as we work on a practice-patient level.

Identification of a plausible mechanism of effective treatment in infancy is not clear-cut, partly because the infant cannot answer for him or herself. Having to rely upon the caregiver may limit the acceptance of evidence as the caregiver may imagine how the infant is responding. The caregiver's interpretation of how the infant feels may be insightful but not totally correct. Moreover, evidence is not the same for everyone and sceptics may require a much higher level of evidence than someone who has seen the effects in action. Providing evidence is the key to acceptance.

The evidence-based model is embraced by the chiropractic profession. Long gone are the days when the fundamentalist chiropractic profession believed in manipulation as a panacea for all mankind's ills, reliant upon Palmer's (1910) ideas that blockage (subluxation) of a certain life force was a primary cause of illness. The chiropractic profession subscribes to Engel's proposed (1977) biopsychosocial model (Fava and Sonino, 2008) of health and disease that embraces a multifactoral cause (biological, psychological, social). For children, another model may be more appropriate for musculoskeletal disorders and pain comprising components of mechanical, chemical and central sensitivity (Breen et al., 2012; Breen, 2013) and a lesser emphasis on the psychological and social domains.

### **C. What are the costs of chiropractic therapy for the treatment of inconsolable crying?**

This data lead to the obvious question as to whether chiropractic treatment is associated with benefits that justify the costs, since it is not commonly covered by the National Health Service in the UK. That said, health care has costs, whether paid by the government or by the individual. Although it is uncommon for clinicians to be quizzed about the economic evaluation of their treatments (Phillips, 2008), particularly where the clinician's services are covered by a national health plan, it is increasingly appropriate to ask this question, when prudence in health care expenditures is required.

Does an evidence-based framework involve not only the most efficacious treatment, but also a cost-conscious plan of management? Avoidance of unnecessary tests and negative adverse events may be more inherent in some types of treatment than others. Part of evidence base is the choice of the patient. In the case of paediatric patients, parents choose and it appears that parents want CAM therapies and they also would like their doctors to work together (Ben-Arye et al., 2010). Carlton, Johnson and Cunliffe (2009) found that GPs were a strong influence. Further evaluation of the relative costs of all of the options might help to identify an efficient choice for a particular condition or malady.

Cost-effectiveness has been defined as the top-up cost required per additional unit of health benefit produced as compared with the next most effective treatment (Kim, 2010). This issue is influenced by the seriousness of the condition under treatment, the costs of the condition if untreated, the efficacy of the treatments, durability of treatment along with patient satisfaction with the treatment. (Chapters 1, 8 and 9). It should be kept in mind that any specific therapy may be part of a total treatment plan and total costs may be difficult to identify. Parents choose specific therapies and all have a cost, some easier to establish than others. For example, parents may choose over-the-counter medication, which has a specific cost per unit, but it may be difficult, if not impossible, for researchers to determine how many units were actually given to the child. Also, cost-effectiveness is evaluated in a specific way, generally along-side a RCT, whereas determining the cost-burden of a specific condition is additive in nature, counting up the costs of various types of care and comparing them.

Parents in the USA spent \$149 million (~£90 million) for CAM therapies or remedies for their children in 1996 (Yussman et al., 2004). That was 17 years ago and by all counts, CAM has grown significantly since then (Barnes et al., 2008). If 3.7% was allotted to chiropractic (Birdee, 2010), the portion was \$5.7 million (£3.3million) in 1996, which is equivalent in

inflationary terms to \$8 million (or £5 million) in 2012 (inflation calculator- [www.ThisIsMoney.co.uk](http://www.ThisIsMoney.co.uk)) spent on chiropractic manual therapy for children. Manual therapy usage has increased since then (Birdee, et al., 2010) and economics should be reconsidered.

Manual therapy has been found to be cost-effective (Doran et al., 2010; Korthals-de Bos et al., 2003; Williams et al., 2004; Gurden et al., 2012) in adults. However, there has been no attempt at investigation of costs of chiropractic manual therapy for the treatment of the infant inconsolable nocturnal crying syndrome (infant colic). In the UK, there are direct costs to the NHS of treating the baby as well as indirect costs of family travel, lost sleep, lost work time and potential costs of low self-efficacy, depression, anxiety, exhaustion, anger, marital distress and possibly even child maltreatment (Papousek et al., 2008). An estimate of the direct NHS costs of treating the crying baby less than 12 weeks of age in 2001 in the UK was £65 million per annum (Morris et al., 2001). No therapeutic benefits were reported as accruing from those costs (Morris, et al., 2001).

Twelve years on, a new cost assessment is appropriate. Bromfield and Holzer in 2008 discussed the array of treatments possibly accessed by parents for infants with colicky symptoms (Appendix IX). Parents access GPs, nurses, hospital based paediatricians and CAM practitioners (McCallum et al., 2011). Table 14 shows costs associated with routine management that the parent may access from the NHS or recommended by the NHS during an episode of infant colic. There is also a cost for maltreatment calculated relative to the expected numbers within the population. Full life-time costs have not been added in, although they have been itemised. This hopefully would involve only a very small number of cases. It must be noted that excessive crying is the predominant reason parents give for maltreatment of their child and the child less than one year of age is the most commonly abused member of society (Carbaugh, 2004).

One of the longest-term costs of ill-health is a change from breastfeeding to formula feeding. A diagnosis of colic has been shown to predict shorter duration of breastfeeding (Howard et al., 2006), and this, perhaps, could be argued to be the greatest cost of all, since it predicts not only higher medical costs in the first year of life but also lifelong (Ball and Wright, 1999). There were 795,249 infants in the UK in mid-2010 (Office for National Statistics, 2011). Freedman et al. (2009) calculated that 21% of infants present to primary care for excessive crying and this resulted in the 167,000 infants (calculated to the nearest 100) used for a cost analysis in Table 14.

Type of management	Cost per child	Cost per cohort
NHS consultation (mean 4.25/baby), mean costs of midwife, Health Visitor, GP	£27.50/average (mean 4.25 visits) = £116.88/child	£19,518,025
Accident and Emergency visit(1)	£131/visit (no admittance)	\$21,877,000
Paediatrician (1 visit/baby)	£194/visit (out-patient medical specialist)	£32,398,000
Medications prescription-(n=1)	£41/child	£6,483,940
Medication-over the counter-(n=3)	Mean £6.95/unit x 3 units =£20.85/child	£3,481,950
*Hypoallergenic formula for one week trial for all children	One week of formula for all colic children = £160/week /child	26,720,000; (costs higher for those who require formula for more than one week)
*Non-allergenic formula (1%)	£31.61/child	£5,278,870 ( £3161/child, calculated for 1% of children)
Change from breastfeeding to formula feeding	Mean £349.49/child in additional health care costs in the first year in 2013	£58,364,830
Non-accidental injury (NAI)	Affects 11.6/100,000 = 19 in this cohort; £12.28/child first year, £1000/child lifetime	£2,052,000/first year (~£170 million in a lifetime; mean cost £1000/child lifetime)
Total potential costs, using NICE guidelines for care and evidence of health care usage	Cost per child is £1,057 in first year without full change in formula but single week's trial per guidelines (no lifetime additions for NAI)	£176,624,615/cohort (includes one week trial of formula, not full change to formula feed needed in small number cases; no additions for lifetime NAI)
<p>GP costs/visit from Unit Costs of Health and Social Care, UK, 2011 was £36, mean for all practice practitioners was £27.50 so lower number used; A&amp;E costs per visit with no admittance national average was £131 from 7.1 hospital costs in Unit Costs of Health and Social Care in 2010 (p119); Prescription cost/consultation was £41 from Unit Costs of Health and Social Care 2011, p. 149. Costs of loss of breastfeeding calculated in 1999 units by Ball and Wright (1999) and adjusted to 2012 UK currency with inflation calculator. Clinical Knowledge Summary (CKS) guidelines recommend 1 week trial simethicone drops, 1 week trial of hypoallergenic diet and 1 week trial lactase (NHS Institute for Innovation and Improvement: CKS:safe, practical clinical answers fast (<a href="http://www.cks.nhs.uk/colic-infantile#2898400007">www.cks.nhs.uk/colic-infantile#2898400007</a>)). *Formula cost data calculated by Taylor et al., 2012. NAI=non-accidental injury.</p>		

**Table 14: Costs of routine care for excessively crying infant in the UK per unit (2010)**

Table 15 differs from Table 14 in that it depicts per unit costs that parents might choose for their afflicted child and are not necessarily included in NHS guidelines or clinician recommendations. In order to most easily compare costs, it uses both unit costs and costs for the full cohort of infants who might suffer with excessive crying. Further, it depicts costs of an episode of care for the time frame of the condition. Since the condition is said to self-resolve or divert to other symptoms by 26 weeks of age, for the purposes of this cost analysis, treatment episode was considered to be five months (20 weeks, considering the condition starts at 1-2 weeks of age). Lactase was given a shorter time frame as most clinicians agree lactose intolerance is rare and transitory in nature in this age group (Shergill-Bonner, 2010). In short, the reader may pick and choose which of the costs and time frames are most relevant and add only those together for a final cost assessment.

<b>Type of Management</b>	<b>Cost per unit</b>	<b>Total cost of episode</b>
UK Private health care (Mean contacts 4.25)	£164.41/child	47,898,315
Private chiropractic care (Mean worldwide) (Mean contacts: 4)	£132.26/child	£11,043,710
Simethicone (5 months)	£2.14/unit	£14,293,452
Other over-the-counter products: Dentinox (5 months)	£4.19/unit	£13,994,600
Gripe water (5 months)	£3.49/unit	£16,232,400
Lactase (10 weeks, one unit per 2 weeks)	£9./unit	£15,030,000
Hypo-allergenic feed, cost per child following GP evaluation	£1853*/child	£49,475,100
<b>Total potential costs</b>	<b>£1005/child</b>	<b>£167,967,577million /cohort /year</b>
*cost data calculated by Taylor et al., 2012; Hospital and specialist services not included; costs should not all be added as all would not likely be utilised.		

**Table 15: Costs of specific types of management of infant colic in 2010**

A particularly helpful way to determine cost is to follow the costs of care as they occur in a randomised controlled trial (Hollinghurst et al., 2008). This allows costs to be compared with efficacy as determined in that trial. In a cost analysis paralleling the RCT presented in this thesis, Table 16 gives actual costs incurred in a randomised controlled trial for infant colic (study VII). Cost effectiveness profiling was not completed during this trial.

Type of management	Cost per infant	Total for cohort (100)	Total costs extrapolated to 167,000 cases
Medical visit to rule out illness and make referral for manual therapy	£27.50	£2750	£4,592,500
Chiropractic treatments, mean of 4 per child	£58	£5800	£9,686,000
Total costs	£85.50	£8550.	£14,278,500
Costs based upon GP office visit from GP costs/visit from Unit Costs of Health and Social Care, UK,2011, mean for GP was £36; mean for all practice practitioners was £27.50 and this number was used as it was in NHS studies; Chiropractic treatment based on actual clinic costs during RCT study, 2010-2012, Anglo-European College of Chiropractic, Bournemouth, Dorset, England, UK.			

**Table 16: Costs of care associated with Miller, Newell and Bolton 2012 RCT for infant colic**

The efficacy of the trial results are published elsewhere (Miller, et al., 2012) and can be viewed in Appendix VII. In the RCT, there was a mean change in the intervention group of (minus) -2.4 to -2.8 hours of crying by day 10 (which occurred before 10 weeks of age). Taking the average reduction of 2.6 hours, this is a cost of £32.88 (\$50 US) per hour reduction of inconsolable crying. The NNT was 3, showing good effectiveness of the chiropractic manual therapy intervention. At the end of the trial, infants cried less than 2 hours per day and this may be considered clinically meaningful as colicky babies do not normally cry less than two hours daily until 16-26 weeks of age or older (Keefe et al., 1996).

If all the afflicted children in the UK in 2011 were given this treatment for an episode of care, the total cost would be £14,278,500. Success is not guaranteed. However, evidence suggests that taking a crying baby to a chiropractor results in less crying (Hughes and Bolton, 2001).

Risk as well as benefit must enter the analysis. There has been one report of an adverse event from chiropractic treatment of an infant presented to a chiropractor for colic (Wilson et al., 2012) and this is in dispute (Fuhr and Fischer 2013). There is, over-all, very little evidence of harm from chiropractic manual therapy in the treatment of children (Humphreys, 2010; Adams et al., 2013). Close monitoring of the baby and family is a hallmark of this type of management (Hawk, et al., 2009). Close monitoring over the difficult weeks may be one of the benefits for the family and society.

To compare current costs of chiropractic treatment with the total costs of infant colic to the NHS the last time an official cost analysis was done (Morris et al., 2001), using chiropractic care could have resulted in a savings of £50,721,500 in 2001 (approximately £60 million in 2012 currency). In 2010, the cost of an episode of chiropractic care is approximately the cost of an episode of treatment with simethicone alone. If multiple types of health care were subsequently not accessed by the family, it might save up to £150 million per year. This is a small number when compared to the NHS annual budget of £106 billion and perhaps should be looked at more in light of helping families than pure economic savings. It might be worthy of a small observational trial in part of the country to begin to determine whether there are any benefits in terms of costs or improved outcomes for the child or family by using manual therapy. There may be benefits for the health care system which dedicates many resources to this condition.

Once an excessively crying infant has been determined to be healthy and suffering from no illness, a relatively low cost choice of treatment may be a short trial of chiropractic manual therapy. So far, the performance of chiropractic care is better than other therapies (Lucassen, 2010; Dobson et al., 2012) while in a worst case scenario, a baby not helped has extremely low risk of coming to any harm with manual therapy (Humphreys, 2010). More studies of higher quality are needed to test the concepts presented herein.

In conclusion, it may be appropriate to conduct an early musculoskeletal assessment of newborns. A short course of chiropractic manual therapy may be beneficial should neuromusculoskeletal imbalances or dysfunctions be found, or if inconsolable nocturnal crying of infancy is diagnosed. This thesis suggests that chiropractic manual treatment has shown some promise of effectiveness and that costs are roughly equivalent to the most commonly used, but ineffective, pharmacological therapy. The scope of the problem of the excessively crying infant demands that further research to establish effectiveness and cost-effectiveness of all types of care are required.

## Chapter 13. Conclusions

The studies in this thesis add evidence to the global problem of the excessively crying infant (infant colic). Since most researchers would agree that the term "infant colic" is not representative of the condition, this thesis proposes 'inconsolable nocturnal crying syndrome' (INCS).

Researchers have been unable to provide an aetiology for the condition nor discover a treatment that reduces either its short-term or long-term negative outcomes. This thesis introduced the possibility that the musculoskeletal system might be the cause of a pain syndrome, stemming from a difficult birth, as most research agrees that the key risk factor for the condition is a traumatic birth (Zwart et al., 2007).

Nevertheless, manual therapists in general and chiropractors in particular have been slow to advance research for the paediatric patient, probably thinking that research into pain in adults could be applied to children. This PhD thesis revealed that it is possible, ethical, practical and relevant for the chiropractic profession to research the problems of children related to musculoskeletal disorders. No children were especially recruited for these studies as they were routinely presented by parents looking for answers to their child's problems, commonly referred by their primary care practitioner. This thesis demonstrates the relevance of the profession to the musculoskeletal and behavioural health of children, particularly as it pertains to activities of daily living. It is hoped that it may begin a cascade of research into the musculoskeletal problems of children.

This research may be of use to other professions and families, for example:

1. Families may wish to try a short (two week) trial of chiropractic manual therapy for an infant with INCS, as evidence suggests at least some benefit, if not full recovery, is likely.
2. Physicians may wish to refer such children to a chiropractor for a short trial of therapy.
3. Health care researchers may want to conduct a Delphi study to improve categorisation, sub-grouping and naming or diagnosing infants suffering from excessive crying disorders among an interdisciplinary set of health care professionals.
4. Health care researchers should investigate minimally important differences in clinical outcomes for families afflicted by this condition so that the exact and most appropriate outcomes are measured.

Steps to strengthen the evidence provided by the studies in this thesis include:

1. There is promising evidence that chiropractic manual therapy is efficacious in both the short- and long-term for the management of INCS. Further studies should be designed to randomise cases against routine conventional care and to follow cohorts through to late childhood to identify long-term benefits.
2. Cost-effectiveness studies using RCTs should compare chiropractic manual therapy with routine conventional care.
3. Large cohorts of children treated by chiropractors should be studied for adverse effects.
4. *A priori* subgroups should be studied to determine robustness of the proposed sub-groups of excessively crying babies.
5. The one-page QUIC survey form should be tested for sensitivity in infants with INCS.

In conclusion, the papers amalgamated in this thesis suggested that infants are presented to chiropractors by their parents often with a referral from their primary care practitioner, primarily for the problem of excessive crying of infancy. A ten-day trial of low force manual therapy resulted in statistically significantly less crying along with improved sleep in the child, and reduced stress reported by the parent. These outcomes were confirmed with reliability studies of the crying diary and QUIC survey. No adverse events occurred due to this treatment during the study series. A next key step for improved quality and depth of investigation of this common problem is interdisciplinary cooperation to develop more effective management strategies for this common condition afflicting large numbers of infants.

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